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MONOGRAPHIC MEDICINE

VOLUME VI

THE PROGNOSIS OF INTERNAL DISEASES

BY

HENRY L. ELSNER, M.D., LL.D.

PROFESSOR OF MEDICINE, COLLEGE OF MEDICINE, SYRACUSE UNIVERSITY

NEW YORK AND LONDON
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1917

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"But the power of prognosis is at once the most complete and the most easily understood proof of the reality of knowledge. As soon as an eclipse could be correctly predicted, astronomy was proved to be a true science; and, particularly, we find that nothing so much secures the confidence of patients as a prediction which proves true" (Pye-Smith).

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Preface

The purpose of this book is to bring reassurance and comfort to the physician, and through him greater benefit to the patient.

The study of prognosis begets confidence.

"He heals best who is most certain of the course of disease." This is an aphorism which is incontrovertible; hence the physician who would give a reliable forecast of disease is at once forced to a consideration of underlying conditions. He must think clearly, must have a fundamental knowledge of physiologic processes, must study the perversion of these—pathologic conditions—must be able to interpret the meaning of subjective and objective manifestations, must be able to determine the reciprocal relations of Constitution, Resistance and Heredity; he must view the body as a whole and he must recognize the fact that medical prognosis is exceedingly complex and therefore demands the consideration of multiple data.

Medical prognosis includes the scientific survey of the entire field of Medicine.

The author and the publishers hope that this work on "The Prognosis of Internal Disease," the first systematic treatise on this subject to be presented to the medical profession, will stimulate the workers in the field of medicine to the acquisition of such fundamental knowledge as is needed for the reliable forecast of disease as it presents in practice.

These facts, and the study of the meager literature of the subject of Prognosis, have encouraged the author during the many years of his professional activity to accumulate the material upon which his conclusions are based, and finally to launch this work.

The author fully appreciates the fact that the study of medical prognosis must often forcibly impress the profession with the limitations of its art; on the other hand, it is made conscious of the possibilities of medicine by the association of pathologic knowledge with keen diagnostic and therapeutic ability, tempered with tact and the humane spirit of the true physician.

The enormous advances which have resulted from animal experimentation, including vivisection, and the refinements of diagnosis aided by the newer sciences, particularly bacteriology, have completely changed our conception of many diseases.

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The devotion of a band of unselfish and patient workers in the laboratories and among the infected in far-off countries, many of whom welcomed hardships and even sacrificed their lives that medical truths might be established, has led to the prevention of some diseases and favorably changed the forecast of others.

The author has aimed to establish the urgent necessity in practice of correlating all available knowledge that *safe conclusions* for diagnosis, prognosis, and treatment may be reached, and he has sought to impress the further fact that the practical physician must brace himself against one-sided reasoning, and always place the greater reliance upon the subjective and objective features of the individual case, to which he should add (and aim to interpret correctly) the results of laboratory investigation.

The author wishes to express his appreciation of the confidence which during more than a third of a century has been extended to him by his professional colleagues. Without their support this book would have been impossible. Their friendship and encouragement have been important factors in leading him to the completion of this monumental task.

To the publishers, the author extends his thanks and his appreciation for their uniform courtesy and material assistance.

To the reader, the author delivers the following pages with the hope that they will often reassure, comfort and stimulate him.

If his friends and the readers find only a fraction of the pleasure in the study of "The Prognosis of Internal Disease" that the author has enjoyed during the years of its production, he will feel sufficiently rewarded.

HENRY L. ELSNER.

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Contents

Section I. Specific Infectious Diseases

PAGE

A. Protozoan Infections 15

1. Syphilis 16

I. Acquired Syphilis 16

Specific Diseases of the Cardiovascular System . . 26

Arteritis 26

Aortitis syphilitica 27

Heart Syphilis 28

Phlebitis syphilitica 29

Syphilis of the Liver 30

Syphilis of the Kidney 31

Syphilis of the Testicle and Epididymis 32

Syphilis of the Bones and Joints 32

Syphilis of the Muscles (Myositis) 32

Syphilis of the Respiratory Organs 32

Nasal Syphilis 32

Laryngeal Syphilis 33

Bronchial and Tracheal Syphilis 33

Syphilis of the Lung 33

Syphilis of the Spleen 33

Syphilis of the Digestive Tract 34

Syphilis of the Rectum 34

Syphilis of the Stomach 34

Syphilis of the Esophagus 34

Syphlis of the Intestines 34

Syphilis of the Nervous System 35

Syphilis of the Spinal Cord 35

Syphilitic Peripheral Neuritis 37

Cerebral Syphilis 38

Late Tertiary Lesions—so-called "Metasyphilitic Diseases" 44

I. Tabes dorsalis—Locomotor ataxia . . . 45

II. Taboparesis 61

III. General Paresis 62

Digitized by Google

PAGE

2. Congenital Syphilis 65
Syphilis and Marriage 68
Syphilis and Life Insurance 68
The Fate of Syphilitics and Their Children . . . 69
Carriers of Treponema pallidum 70
II. Malaria 72
1. Intermittent Malarial Fever 73
(a) Quotidian Type 73
(b) Tertian Type 73
(c) Quartan Type 73
(d) Irregular Intermittent Fever . . . 73
2. Remittent Malarial Fever 74
(a) Aestivo-autumnal fever 74
(b) Pernicious Malarial Disease 74
(c) Black Water Disease or Hemorrhagic Malarial Fever 76
3. Chronic Malarial Cachexia 76
4. Mixed Types of Malarial Fever 77
5. Malarial Neuralgia 77
6. Malarial Complications 77
III. Amebic Dysentery—Amebiasis 78
IV. Trypanosomiasis 81
V. Relapsing Fever 82
VI. Leishmaniasis 83

B. Bacterial Diseases 84
I. Typhoid Fever 84
II. Typhus Fever 117
III. Paratyphoid Disease 121
IV. Influenza 124
V. Pyogenic Infections—Septicemia—Pyemia . . . 130
VI. Diphtheria 134
VII. Pneumococcus Infection 145
1. Lobar Pneumonia 145
2. Bronchopneumonia 169
VIII. Erysipelas 173
IX. Epidemic Cerebrospinal Meningitis 177
X. Whooping-cough 186
XI. Gonococcus Infections 189
1. Gonococcus Endocarditis 190
2. Gonococcus Arthritis 192
XII. Bacillary Dysentery 193
XIII. Malta Fever 196

Digitized by Google

PAGE

XIV. Asiatic Cholera 197
XV. Plague 201
XVI. Tetanus 206
XVII. Anthrax 209
XVIII. Glanders 212
XIX. Leprosy 214
XX. Tuberculosis 216
History 217
1. Acute Miliary Tuberculosis 222
I. Typhoid Form 223
II. Pulmonary Form 224
III. Meningeal Form 224
2. Pulmonary Tuberculosis 226
I. Acute Pneumonic Tuberculosis . . 227
II. Chronic Pulmonary Tuberculosis . 229
III. Fibroid Phthisis 244
3. Tuberculous Pleurisy 247
4. Parotid Tuberculosis 249
5. Nasal Tuberculosis 250
6. Laryngeal Tuberculosis 249
7. Tuberculosis of the Digestive Tract . . 252
8. Tuberculous Peritonitis 257
9. Tuberculosis of the Pancreas . . . 262
10. Tuberculosis of the Spleen 262
11. Tuberculosis of the Suprarenal Gland—Addison's Disease 263
12. Tuberculosis of the Lymphatic Glands . . 265
13. Genito-urinary Tuberculosis 267
14. Cardiovascular Tuberculosis 274
15. Tuberculosis of the Nervous System . . 277
XXI. Rheumatic Fever (Acute Polyarthritis) 278
XXII. Tonsillitis 292
(a) The Influence of the Tonsil on Prophylaxis and Prognosis 292
(b) Acute Follicular Tonsillitis 293
(c) Phlegmonous Tonsillitis (Septic) . . . 297
(d) Acute Suppurative Peritonsillitis (Quinsy) . 297
(e) Vincent's angina 298
(f) Chronic Tonsillitis (Adenoids) 299
XXIII. Metastatic Parotitis 300

C. Non-Bacterial Fungus Infection 301
Actinomycosis 301

Digitized by Google

PAGE

D. Diseases Due to Metazoan Parasites 303
1. Cestodes 304
(a) Tenia solium 304
(b) Tenia saginata or Mediocanellata 305
(c) Bothriocephalus latus 305
(d) Tenia echinococcus (Hydatid Disease) . . . 306
2. Nematodes 309
(a) Ascaris lumbricoides 309
(b) Oxyuris vermicularis 309
(c) Ankylostomiasis 310
(d) Tricocephalus dispar 312
(e) Trichinosis 312
(f) Filiariasis 315
3. Trematodes 316
Bilharzia haematobia 316

E. Infections of Unknown or Doubtful Origin 317
I. Poliomyelitis 317
1. Acute Poliomyelitis (Infantile Paralysis) . . 317
2. Chronic Poliomyelitis 326
II. Scarlet Fever 327
III. Smallpox 333
IV. Varicella 341
V. Measles 342
VI. German Measles 346
VII. Yellow Fever 347
VIII. Foot and Mouth Disease. 349
IX. Ephemeral Fever 350
X. Infectious Jaundice (Weil's Disease) 350
XI. Sweating Sickness 351
XII. Herpetic Fever 352
XIII. Fourth Disease (Duke's Disease) 352
XIV. Epidemic Parotitis 352
XV. Glandular Fever (Pfeiffer's Disease) 353
XVI. Hydrophobia 354
XVII. Dengue 356

Section II. Diseases of the Respiratory Apparatus

A. Diseases of the Nose 357
1. Acute Catarrhal Rhinitis (Coryza) 357
2. Hay Fever 358
3. Epistaxis 359

Digitized by Google

PAGE

B. Diseases of the Larynx 360
1. Acute Laryngitis 360
2. Chronic Laryngitis 361
3. Edema of the Larynx 362
4. Laryngismus stridulus 362
5. Tuberculous Laryngitis 363
6. Syphilitic Laryngitis 363

C. Diseases of the Bronchi 363
1. Acute Bronchitis 363
2. Chronic Bronchitis 365
3. Bronchiectasia 366
4. Bronchial Asthma 368
5. Fibrinous Bronchitis 373
6. Whooping-cough 373

D. Diseases of the Lung 373
1. Circulatory Disturbances of the Lung 373
Congestion—
(a) Active 373
(b) Passive 374
(c) Pulmonary Edema 375
2. Pulmonary Hemorrhage 376
(a) Hemoptysis 376
(b) Pulmonary Infarct 378
3. Chronic Non-tuberculous Pneumonia 379
(a) Chronic Pneumonia 379
(b) Chronic Interstitial Pneumonia 379
(c) The Pneumonokonioses 380
4. Emphysema 382
5. Gangrene of the Lung 385
6. Abscess of the Lung 386
7. Neoplasm of the Lung 387

E. Diseases of the Pleura 389
1. Pleurisy 389
(a) Fibrinous Pleurisy 389
(b) Serofibrinous Pleurisy 389
(c) Purulent Pleurisy 392
(d) Tuberculous Pleurisy 395
(e) Chronic Pleurisy 395

Digitized by Google

PAGE
2. Hydrothorax 396
3. Pneumothorax 396
4. Mediastinal Disease 399

Section III. Diseases of the Circulatory Apparatus

A. Arteriosclerosis 402

General Consideration:
1. Age 404
2. Heredity 405
3. Syphilis 405
4. Worry and Stress 405
5. Alcohol 405
6. Lead 406
7. Tobacco 407
8. Infection 407
9. Occupation 407
10. Overeating 409
11. Mechanical Factors 409
12. Chemical and Toxic Factors 409
13. Hypertension 410
14. Kidney Invasion 411
15. Coronary, Myocardial, Endocardial and Other Heart Lesions 411
16. Vascular Crisis (Spasm) 414
17. Cerebral, Spinal and Peripheral Changes . . . 416
18. Blood Pressure Study of Arteriosclerosis (after the stage of hypertension) 416
19. Thrombosis 418
20. Ocular Changes 418
21. X-ray Examination 419

B. Aneurism 420
1. Aneurism of the Ascending Portion of the Arch of the Aorta 423
2. Aneurism of the Transverse Portion of the Arch of the Aorta 423
3. Aneurism of the Descending Portion of the Arch of the Aorta 424
4. Aneurism of the Descending Thoracic and Abdominal Aorta 424

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PAGE

5. Aneurism of the Celiac Axis 425
6. Aneurism of the Coronary Artery 425
7. Aneurism of the Pulmonary Artery 425
8. Aneurism of the Subclavian Artery 425

C. Diseases of the Pericardium 426

1. Acute Pericarditis 426
2. Adherent Pericardium 430
3. Chronic Pericardioperitonitis 432
4. Hydropericardium 433
5. Hemopericardium 433
6. Pneumopericardium 434
7. Neoplasms of the Pericardium 434

D. Congenital Defects of the Heart 435

1. Stenosis of the Pulmonary Orifice 435
2. Defective Ventricular Septum 438
3. Perforate Foramen ovale 438
4. Dextrocardia 438
5. Stenosis of the Aortic Orifice 438
6. Insufficiency and Stenosis of the Mitral and Tricuspid Valves 439
7. Transposition of the Aortic and Pulmonary Artery: Perforate ductus arteriosus and Premature Closure . . 439

E. Myocardial Diseases 441

1. Acute Purulent Myocarditis 442
2. Acute Interstitial Myocarditis (Parenchymatous) . . 443
   (a) Simple Acute Interstitial Myocarditis . . . 443
   (b) Acute Septic Interstitial Myocarditis . . . 443
3. Chronic Myocardial Insufficiency 443
   (a) Fibroid Degeneration (including the Arhythmias) 443
   (b) Fatty Heart 452
   (c) Fragmentation and Segmentation 454
   (d) Brown Atrophy 454
   (e) Coronary Sclerosis (Angina pectoris) . . . 454
   (f) Senile Heart 460
4. Hypertrophy and Dilatation 460
   (a) Overstrain 460
   (b) Hypertension 461

Digitized by Google

PAGE

(c) Hypertrophy — Secondary to Lung Disease, Asthma, Kyphosis, Fixed Thorax and Non-valvular Heart Lesions 462
(d) Hypertrophy—with Masturbation, Uterine Fibroids and Hyperthyroidea 462
5. Stokes-Adams Disease 463
6. Syphilis of the Heart 464
7. Heart Weakness Due to Insufficient Exercise . . . 464
8. Inherent Muscular Weakness 465
9. Insufficiency with the Anemias, Metabolic Faults and Toxic States 465
10. Neoplasms 465
11. Parasites of the Heart 466
12. Rupture of the Heart 466
13. Aneurism of the Heart 467

F. Endocarditis 468

1. Acute Endocarditis 469
(a) Simple Acute Endocarditis 469
(b) Septic Endocarditis 471
2. Chronic Endocarditis 477
1. General Consideration of Chronic Cardiopathies . 477
(a) Hypertrophy 478
(b) Dilatation 480
(c) Decompensation 482
(d) Frequency of Valvular Lesions . . . 483
(e) Sex 483
(f) Heredity and Family History . . . 483
(g) Age 484
(h) Occupation and Social Conditions . . 484
(i) The Influence of Intercurrent Diseases . 485
(j) The Influence of Marriage and Pregnancy on Valvular Diseases 486
(k) The Influence of the Usual Complicating Diseases on the Course of the Chronic Cardiopathies 489
(l) Blood 491
(m) Skin 491
(n) Nephritis 491
(o) Liver 491
(p) Nervous System 492
(q) Dropsies 492

Digitized by Google

PAGE

(r) Pulse 492
(s) Blood Pressure 492
(t) Röntgen Examination 492
(u) Sudden Death and Valvular Anomalies . 493
(v) Anatomic Cure of Valvular Lesions . . 493
(w) Influence of Treatment. 493
(x) Influence of Physical Signs 494
(y) Fate of the Chronic Cardiopaths . . . 494
2. Localization of Valvular Lesions and Their Forms 495
Mitral Insufficiency 495
Mitral Stenosis 497
Aortic Stenosis (Obstruction) 499
Aortic Insufficiency 500
Tricuspid Insufficiency 503
Tricuspid Stenosis 503
Defects of the Pulmonary Valve 503
3. Arteriosclerotic and Syphilitic Endocarditis . . 504
4. Combined Valvular Lesions 504

G. Functional Diseases of the Heart 506
1. Palpitation 507
2. (a) Paroxysmal Tachycardia 508
(b) Simple Tachycardia 510
3. Bradycardia 511
4. Arhythmia 512
5. The Neurasthenic State 512

Section IV. Diseases of the Blood and Hemopoietic Organs

A. Anemia 514
1. Symptomatic Secondary Anemia 514
2. Primary or Essential 517
(a) Chlorosis 517
(b) Pernicious Anemia 519

B. Leukemia 530
1. Leukocytic or Splenomyelogenous Leukemia . . . 530
2. Lymphatic Leukemia 533
3. Acute Leukemia 534
4. Leukanemia 534
5. Mixed Leukemia 535

Digitized by Google

PAGE

C. Hodgkin's Disease—Lymphoblastoma 536

D. Purpura 542

1. Secondary Purpura 542
2. Primary Purpura 543
   (a) Purpura simplex 543
   (b) Purpura rheumatica (Schoenlein's Disease) . 544
   (c) Purpura hemorrhagica (Werlhof's Disease . . 545
   (d) Chronic Purpura 546
   (e) Henoch's Purpura 547
   (f) Hemophilia 548

E. Erythremia 549

1. Primary 549
2. Secondary 551

Section V. Diseases of the Digestive Apparatus

A. Diseases of the Mouth (Stomatitis) 553

B. Diseases of the Salivary Glands 557

1. Mumps—Epidemic Parotitis 557
2. Parotitis 557
3. Mikulicz's Disease 557

C. Diseases of the Pharynx 559

1. Circulatory Anomalies 559
2. Pharyngitis 559
   (a) Acute Pharyngitis 559
   (b) Chronic Pharyngitis 560
   (c) Ulcerative Pharyngitis 560
   (d) Phlegmonous Pharyngitis and Retropharyngeal Abscess 560
   (e) Ludwig's Angina 560

D. Diseases of the Tonsils 562

E. Diseases of the Esophagus 562

1. Acute Esophagitis 562
2. Spasm and Paralysis of the Esophagus 565

Digitized by Google

PAGE

3. Stricture of the Esophagus 566
4. Cancer of the Esophagus 567
5. Rupture of the Esophagus 568
6. Dilatation—Diverticula 568

F. Diseases of the Stomach 570

1. Acute Gastritis 570
2. Chronic Gastritis 572
3. Dilatation of the Stomach—Gastrectasia 576
4. Gastroptosis—Enteroptosis 579
5. Pyloric Obstruction 581
6. Gastric and Duodenal Ulcer 585
7. Cancer of the Stomach 600
8. Hematemesis—Gastrorrhagia 613
9. Gastric Neuroses 615

G. Diseases of the Intestines 619

1. Acute Enteritis—Acute Diarrhea 619
2. Chronic Enteritis—Chronic Diarrhea 623
3. Diarrheal Diseases of Early Childhood 627
4. Celiac Disease—Diarrhea alba—Diarrhea chylosa . . 629
5. Enteroptosis (Glenard's Disease) 630
6. Constipation—Obstipation 630
7. Intestinal Obstruction 633
8. Dilatation of the Colon 640
9. Diverticulum of the Intestine 641
10. Intestinal Cancer and Other Growths 642

H. Diseases of the Appendix 644

Appendicitis 644

I. Diseases of the Peritoneum 659

1. Acute Diffuse Peritonitis 659
2. Chronic Peritonitis 662
3. Tubercular Peritonitis 663
4. New Growths of the Peritoneum 663

J. Diseases of the Liver 664

1. Jaundice 664
   (a) Hepatogenous (Obstructive) Jaundice . . . 664
   (b) Hemolytic (Toxic) Jaundice 668

Digitized by Google

PAGE

(c) Hereditary Splenomegalic Jaundice . . . 670
(d) Icterus neonatorum 670
2. Acute Yellow Atrophy of the Liver 673
3. Circulatory Disturbances of the Liver 676
(a) Congestion of the Liver 676
(b) Diseases of the Portal Vein 678
(c) Diseases of the Hepatic Vein 679
(d) Diseases of the Hepatic Artery 680
4. Cirrhosis of the Liver 681
5. Abscess of the Liver 704
6. Neoplasm of the Liver—Cancer of the Liver . . . 709
7. Fatty Liver 712
8. Amyloid Liver 712
9. Echinococcus of the Liver 714
10. Syphilis of the Liver 714
11. Tuberculosis of the Liver 714

K. Diseases of the Bile Passages and Gall-bladder 714
1. Acute Cholangitis 714
2. Chronic Cholangitis 714
3. Suppurative Cholangitis 715
4. Acute Inflammation of the Gall-bladder 715
5. Chronic Cholecystitis 716
6. Obliterative Cholecystitis and Cholangitis 716
7. Gangrene and Phlegmonous Cholecystitis 717
8. Cancer of the Gall-bladder 717
9. Cholelithiasis 718

L. Diseases of the Pancreas 734
1. Pancreatitis 734
2. Hemorrhage (Pancreatic Apoplexy) 737
3. Necrosis of the Pancreas 738
4. Pancreatic Calculi 738
5. Pancreatic Cysts 738
6. Pancreatic Neoplasms 739

Section VI. Diseases of the Kidney

Anomalies of the Urinary Secretion 741
The Prognostic Significance of:
(a) Albuminuria 741
(b) Casts 749

Digitized by Google

PAGE

(c) Hematuria 753
(d) Uremia 762
(e) Renal Sufficiency Tests 768
(f) Bacilluria—Bacteriuria 774
(g) Chyluria 776
(h) Phosphaturia 777
(i) Oxaluria 779
(j) Indicanuria 780
(k) Urobilinuria 782
(l) Other Substances 785

Diseases of the Renal System 788
1. The Nephropathies 788
(a) Acute Parenchymatous Nephritis 788
Nephritis of Pregnancy 794
(b) Chronic Parenchymatous Nephritis . . . 797
(c) Chronic Interstitial Nephritis 804
(d) Congested Kidney 811
(e) Amyloid Kidney 814
(f) Tuberculous Kidney—Tuberculous Nephritis . 815
2. Surgical Diseases of the Kidney 815
(g) Hydronephrosis 815
(h) Nephrolithiasis 820
(i) Neoplasms of the Kidney (including Hyperneph-roma) 825
(j) Movable Kidney 828
Suppurative Diseases of the Kidney . . 829
(k) Pyelitis 829
(l) Perinephric Abscess 834

Section VII. Diseases of the Nervous System

A. Diseases of the Peripheral Nerves 837
I. Neuralgia 837
(a) Trifacial Neuralgia (Tic douloureux) . . 841
(b) Supra-orbital Neuralgia 841
(c) Occipital Neuralgia 842
(d) Intercostal Neuralgia 842
(e) Mastodynia 843
(f) Phrenic Neuralgia 843
(g) Brachial Neuralgia 843
(h) Lumbar Neuralgia 844
(i) Sciatic Neuritis 844

Digitized by Google

PAGE

II. Peripheral Neuritis 845
1. Mononeuritis 846
(a) Traumatic Neuritis 846
(b) Postoperative Neuritis 846
2. Multiple Neuritis (Polyneuritis) 848
(a) Alcoholic Multiple Neuritis . . . 849
(b) Postdiphtheritic Multiple Neuritis . . 850
(c) Lead Multiple Neuritis 850
(d) Arsenical Multiple Neuritis . . . 852
(e) Multiple Neuritis with Leprosy . . 853
(f) Idiopathic Multiple Neuritis . . . 853
(g) Landry's Ascending Paralysis . . . 854
(h) Puerperal Multiple Neuritis . . . 854
(i) Gonorrheal Multiple Neuritis . . . 855
(j) Neuritis of Tuberculous Origin . . 855
(k) Diabetic Neuritis 855

III. Peripheral Paralysis. 856
Paralysis of the Cranial Nerves 856
(a) Paralysis of Olfactory Nerve . . . 856
(b) Paralysis of Optic Nerve. 857
Optic Neuritis 858
Optic Atrophy 858
Hemianopia 858
Paralysis of Ocular Nerves 860
(c) Paralysis of the Third Nerve 860
(d) Paralysis of the Fourth Nerve . . . 861
(e) Paralysis of the Sixth Nerve 861
(f) Ophthalmoplegia 861
(g) Paralysis of the Fifth Nerve 862
Facial Hemiatrophy 863
(h) Facial Paralysis 863
Bell's Palsy 864
Pontine Facial Palsy 864
(i) Facial or Mimic Spasm 866
(Tic convulsive)
(j) Paralysis of the Auditory Nerve . . . 868
Tinnitus aurium 868
Involvement of Vestibular Nerve . . 869
Vertigo 869
(k) Glossopharyngeal Paralysis 870
(l) Pneumogastric Paralyis 871
(m) Paralysis of the Spinal Accessory Nerve . 871

Digitized by Google

PAGE

(n) Spasm of the Trapezius and Sterno-cleido-mastoid 872
(o) Paralysis of the Hypoglossal Nerve . . 873
(p) Paralysis of the Phrenic Nerve 874
(q) Hiccough—Spasm of the Diaphragm . . 875
(r) Paralysis Due to Lesions of the Brachial Plexus 875
(s) Paralysis Due to Cervical Rib . . . 876
(t) Paralysis of the Posterior Thoracic Nerve . 877
(u) Paralysis of the Circumflex Nerve . . 878
(v) Paralysis of the Median Nerve . . . 878
(w) Paralysis of the Musculospiral Nerve . . 878
(x) Paralysis of the Ulnar Nerve . . . 879
(y) Lumbar and Sacral Plexus Paralysis . . 879
(z) Obturator Nerve Paralysis 880
(aa) Paralysis of the Sciatic Nerve . . . 880
(bb) Paralysis of the Gluteal Nerves . . . 881
(cc) Paralysis of the External Popliteal Nerve . 881
(dd) Paralysis of the Internal Popliteal Nerve . 881
(ee) Paralysis of the Sacral Plexus . . . 882
(ff) Paralysis Due to Lesions of the Cauda equina 882

IV. Tumors of the Peripheral Nerves 883
Neuroma 883
Disseminated Neurofibromata—von Recklinghausen's Disease 883
Elephantiasis neuromatosa 884

B. Diseases of the Spinal Cord and Its Membranes . . . 885

I. Diseases of the Afferent or Sensory System . . . 885
1. Tabes dorsalis 885
2. General Paralysis of the Insane 885
3. Taboparesis 885
4. Herpes zoster 885
5. Hereditary Ataxia (Friedreich's Disease) . . 887
6. Marie's Hereditary Ataxia 888

II. Anterior Diseases—Diseases of the Efferent or Motor Tract 888
1. Poliomyelitis Anterior—Infantile Paralysis . 888
2. Landry's Ascending Paralysis 888
3. Progressive Central Muscular Atrophy . . 888
(a) Progressive (Central) Spinal Muscular Atrophy 889

Digitized by Google

PAGE

(b) Amyotrophic Lateral Sclerosis . . 890
(c) Bulbar Paralysis 891
4. Progressive (Neural) Muscular Atrophy . . 894
5. The Muscular Dystrophies. 895
I. The Muscular Dystrophies of Childhood 896
1. Hypertrophic Muscular Atrophy. 896
2. Atrophic Form 897
II. Erb's Juvenile Progressive Muscular Atrophy 897
6. Myotonia or Amyotonia congenita (Oppenheim's Disease) 898
III. Diseases of the Lateral Columns of the Cord . . . 899
1. Primary Lateral Sclerosis 899
2. Congenital Lateral Sclerosis (Little's Disease) . 900
3. Combined Lateral and Posterior Disease (Ataxic paraplegia) 901
4. Amyotrophic Lateral Sclerosis (Charcot's Disease) 902
5. Erb's Syphilitic Spinal Paralysis 902
6. Secondary Spastic Paralysis 902
7. Amaurotic Family Idiocy (Sachs' Disease) . 903
IV. Indiscriminate Lesions of the Spinal Cord . . . 904
1. Myelitis 904
2. Multiple Sclerosis of the Brain and Spinal Cord 908
3. Pseudomultiple Sclerosis 913
4. Abscess of the Spinal Cord 914
5. Syringomyelia 915
6. Tumors of the Spinal Cord 918
7. Caisson Disease 927
8. Affections of the Blood Vessels 927
(a) Anemia of the Cord 927
(b) Hyperemia of the Cord 928
(c) Spinal Endarteritis—Arteriosclerosis . 928
(d) Spinal Embolism and Thrombosis . . 928
V. Diseases of the Spinal Membranes 930
1. Hemorrhage into the Spinal Membranes and Cord 930
2. Spinal Hematoma 931
3. Spinal Meningitis 931
(a) Spinal Pachymeningitis 932
(b) Hypertrophic Cervical Pachymeningitis . 932
(c) Acute Spinal Leptomeningitis . . . 933
(d) Chronic Spinal Leptomeningitis . . 933
(e) Postbasic Meningitis. 934

Digitized by Google

PAGE

C. Diseases of the Brain and Its Membranes 934
I. Diseases of the Membranes of the Brain . . . 934
1. Pachymeningitis 934
2. Leptomeningitis 937
(a) Purulent Leptomeningitis. . . . 938
(b) Serous Leptomeningitis 942
I. Serous Meningitis . . . 943
II. Acquired Hydrocephalus . . 943
III. Congenital Hydrocephalus . . 944
(c) Chronic Leptomeningitis 946
3. Syphilitic Cerebral Meningitis 947
4. Tuberculous Meningitis. 947
5. Cerebrospinal Meningitis (Epidemic) . . . 947
II. Circulatory Disturbances of the Brain 947
1. Anemia 947
2. Hyperemia of the Brain 949
3. Occlusion of the Cerebral Vessels 953
4. Cerebral Hemorrhage 957
5. Encephalitis 973
6. Cerebral Paralysis of Childhood 977
7. Abscess of the Brain—Suppurative Encephalitis 980
8. Aneurism 987
III. Tumors of the Brain. 988
IV. Parasites of the Brain 1002
V. Cerebellar Diseases 1003

D. Functional and General Diseases of the Nervous System . . 1005

1. Hysteria 1005
2. Traumatic Neurosis 1021
3. Neurasthenia 1025
4. Paralysis agitans 1033
5. Chorea 1037
6. Tetany 1046
7. Epilepsy 1046
8. Migraine 1059
9. Occupational Paralyses and Neuroses. 1064
10. Infantile Convulsions 1065

E. Diseases of the Sympathetic System 1066

Vasomotor and Trophic Disorders 1066
1. Erythromelalgia 1066
2. Raynaud's Disease. 1069

Digitized by Google

PAGE
3. Acroparesthesia 1074
4. Angioneurotic Edema 1075
5. Scleroderma 1077
6. Adiposis dolorosa 1978
7. Intermittent Dropsy of the Joints. 1079
8. Hereditary Edema of the Legs (Milroy's Disease) . 1080
9. Paralysis of the Cervical Sympathetic 1081
10. Irritation of the Cervical Sympathetic . . . 1082
11. Vagotonia 1082
12. Sympathicotonia 1083

Section VIII. Diseases of the Locomotor System

A. Diseases of the Muscles 1084
1. Myalgia—Myositis 1084
2. Progressive Myositis ossificans 1085
3. Thomsen's Disease (Myotonia) 1085
4. Paramyoclonus multiplex 1086
5. Akinesia algera 1086

B. Diseases of the Joints 1088
Destructive Chronic Polyarthritis 1088
(a) Arthritis deformans 1088
(b) Chronic Articular Rheumatism 1088

C. Diseases of the Bones 1093
1. Osteitis deformans (Paget's Disease) 1093
2. Leontiasis ossea 1095
3. Hypertrophic Pulmonary Arthropathy 1096
4. Fragilitas ossium 1097

Section IX. Metabolic Faults

1. Gout 1098
2. Diabetes mellitus 1106
3. Diabetes insipidus 1122
4. Obesity 1124
5. Rachitis 1129
6. Achondroplasia 1131
7. Osteomalacia 1131
8. Scorbutus 1132
9. Multiple Myeloma 1134

Digitized by Google

Section X. Diseases of the Ductless Glands

PAGE

A. Thyroid Diseases 1136
1. Growths 1136
(a) Tumors—Thyroiditis 1136
(b) Goiter 1137
2. Hyperthyroidea 1139
(a) Exophthalmic Goiter 1139
(b) Myxedema, Cretinism 1153

B. Diseases of the Pituitary Gland 1158
1. Hypopituitarism 1158
Infantilism 1158
2. Hyperpituitarism 1158
Acromegaly 1160

C. Diseases of the Suprarenal Gland 1163
Addison's Disease 1163

D. Diseases of the Thymus Gland 1163
1. Hypertrophy 1163
2. Atrophy 1164
3. Status thymo-lymphaticus 1164
Lymphatism 1164

E. Diseases of the Parathyroid Gland 1165
Tetany 1165

F. Diseases of the Spleen 1169
1. Secondary Splenomegaly 1169
(a) Passive Congestion 1170
(b) Abscess 1170
(c) Perforation 1170
(d) Perisplenic Abscess 1170
(e) Perisplenitis or Capsulitis 1170
(f) Tuberculous Spleen 1170
(g) Amyloid Spleen 1170
(h) Syphilis 1170
(i) Uncomplicated Enlargement in Otherwise Healthy Subjects 1170

Digitized by Google

PAGE
(j) Chronic Enlargement with Polycythemia . . 1170
(k) Enlargement with Liver Cirrhosis 1171
(l) Rupture of the Spleen 1171
(m) Cyst of Spleen 1171
(n) Infarct 1171
2. Primary Splenomegaly 1171
(a) Gaucher's Disease (Primary Endothelioma) . . 1171
(b) Banti's Disease—Splenic Anemia 1172
3. Mobile Spleen 1173

Section XI. Intoxications

1. Alcoholism 1175
(a) General Consideration of the Alcoholic Habit. . 1175
(b) Acute Alcoholic Poisoning 1179
(c) Chronic Alcoholism 1180
(d) Delirium tremens 1183
2. Morphinism 1185
3. Cocainism 1187
4. Lead Poisoning 1187
5. Arsenical Poisoning 1193
6. Mercurial Poisoning 1195
7. Carbon Monoxid Poisoning. 1196
8. Pellagra 1197
9. Beriberi 1201
10. Food Poisoning (Ptomain and Leukomain Poisoning) . 1203

Section XII. Diseases Due to Physical Agents

1. Sunstroke (Heat Exhaustion) 1205
2. Caisson Disease 1207
3. Mountain Sickness 1209

INDEX 1211

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THE PROGNOSIS OF INTERNAL DISEASE

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The Prognosis of Internal Disease

General Considerations

Medicine has not grown to its present advanced position in logical sequence.

Prognosis is the prescience of disease, the art of foretelling the progress and termination of disease. The foreknowledge thus obtained is included in the term "prognosis."

Prognosis, therefore, includes a forecast of the patient's future, not only whether the disease is curable, but how long under existing conditions life may be prolonged, what influence the disease is likely to have on his activities and the enjoyment of life, what factors may lead to its advance and what will influence its course favorably; hence it stimulates rational treatment.

Leyden has truthfully said "Prognosis represents the very quintessence of the physician's knowledge."

The *literature* which has accumulated on the subject of the Prognostics of Disease, is comparatively meager. (See Bibliography appended, and full literature in Volumes XI, 1st Series, and XIII, 2nd Series, Index Catalogue of the Library of the Surgeon-General's Office, United States Army).

The history of medicine proves that the disciple of our art Hippocrates, was more concerned with the prognostics of disease than with any other question connected with its study. Prognosis became the first object of all Theory connected with Medicine.

"A glimpse into ancient medical literature shows that more space was devoted to the Prognostics of Disease than is occupied for a similar purpose in the modern compendium" (Neuburger). It is a fact that formerly, prognosis was made without accurate diagnosis, without pathologic knowledge; today prognosis is based not only on subjective symptoms but upon the results of thorough physical examination, the consideration of pathologic conditions, the revelations of the laboratory and a well digested previous history—a consideration of all of the features made clear by thorough investigation. This is not all as we shall see; the paramount facts are also offered by the picture which the patient

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presents. A projection upon the diagnostic screen is made, not from the study of text books or monographs, but as a result of years of experience, painstaking analysis and correct reasoning.

Prognosis is often made without accurate diagnosis or positive knowledge of the anatomic lesions, and yet it proves fairly valuable for the immediate future in important cases, pending the acquisition of exact knowledge gained from further study of the individual case.

Hippocrates' rules of practice were based on experience; he was, as his critics have said "the physician of experience and common sense." "What he appears to have studied with particular attention is the natural history of diseases, that is to say, their tendencies to a favorable or fatal issue; and without this knowledge, what can all medical practice be but blind empiricism?" . . . "The physician who cannot inform his patient what would be the probable issue of his complaint, if allowed to follow its natural course, is not qualified to prescribe any rational plan of treatment for its cure" (Francis Adams). Hippocrates was fully conscious of the *fallaciousness of experience* and "therefore never exempts the apparent results of experience from the strict scrutiny of reason." To prove this great truth he made the following, *the first of his aphorisms:*—

Aphorisms of Hippocrates (I):—

"Life is short, and the Art long; the occasion fleeting; experience fallacious, and judgment difficult. The physician must not only be prepared to do what is right himself, but also to make the patient, the attendants, and externals co-operate."

Galen's Commentary on this aphorism shows that he interpreted it as meaning "The occasion is fleeting, experiment is dangerous and decision is difficult."

Galen remarks that it is "hazardous to experiment in a case which involves the life of a human being, and that it is difficult to catch the truth in medicine, as is evident from the circumstances of the profession being divided into so many opposite sects" (Adams).

Hippocrates was conscious of the *power of Nature* to cure disease. He upheld the principle that *"Nature is the physician of diseases"* (Hippocrates). *"Nature although untaught and uninstructed does what is proper."* Sydenham placed his stamp of approval upon these philosophical tenets by quoting them frequently, while Galen's Commentary remains a classic, full of interesting and profitable data, "a fine specimen of the medical philosophy of the ancients."

Herophilus (300 A. D.) was the first commentator on Hippocrates of whom we have any record; unfortunately his Commentaries were never preserved so far as we know. He was also the first to study the *character of the pulse.*

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It is of interest to note that no mention is made in the "Books of the Epidemics" on the characters of the arterial pulse and contagion. Hippocrates, as well as his contemporary Thucydides, must have appreciated the *contagiousness* of the *plague* which the latter described clearly, and taught that the disease was contagious.

Adams' conclusions concerning the authenticity of the works of "The Father of Medicine" may be accepted as being as near the truth as we can ever hope to get:

1. "All the authorities, ancient and modern, who have investigated the question regarding the genuineness of the works which have come down to us under the name of Hippocrates, are agreed that a considerable portion of them are not the production of the author himself."

2. "It is almost universally admitted that the following treatises are genuine, viz:—

The Prognostics
On Airs, et cetera
On Regimen in Acute Disease
Seven of the Books of Aphorisms
Epidemics I and III
On the Articulations
On Fractures
On the Instruments of Reduction
The Oath"

Adams further holds that it may be conceded with considerable certainty that the following treatises are genuine though the "evidence in their favor is not so strong as it is with regard to the preceding list:—

On Ancient Medicine
On the Surgery
The Hand
On Ulcers
On Fistulae
On Hemorrhoids
On the Sacred Diseases"

The first "Prorrhetics" and the "Coacae Praenotiones" probably antedated the time of Hippocrates.

"It appears to me a most excellent thing for the physician to cultivate prognosis; for by foreseeing and foretelling in the presence of the sick, the present, the past, and the future, and explaining the omissions which patients may have been guilty of, he will be the more readily believed

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to be acquainted with the circumstances of the sick, so that men will have confidence to entrust themselves to such a physician. And he will manage the case best who has foreseen what is to happen from the present state of matters" (Hippocrates).

The Book of the Prognostics continues the most learned systematic consideration of the subject which was included in fragmentary references to but few individual diseases until 1601 when Prosper Alpinus, Professor of Medicine at Padua, published a most remarkable dissertation on Prognostics "in confirmation of the Hippocratic method" with the title "De Praesagienda Vita et Morte Aegrotantium," in seven volumes. The work was translated by R. James, M.D., and published in London in 1746 with an introduction by the renowned Boerhaave, taken from an edition of Alpinus published in Leyden in 1709. Since that day there has been no attempt to present a systematic work by a single clinician dealing with the leading feature of all internal diseases which bear upon their prognosis.

J. Harvey published his "Praesagium Medicum or the Prognostick Signs of Acute Diseases, Established by Antient Observation and Explained by the Best modern Discoveries" in London in 1706; a work which created a sensation in the profession.

The leading publications dealing with the separate consideration of the prognostics of disease during the nineteenth century were "Traite Elementaire de Diagnostic de Prognostic, et cetera," par Leon Rostan, Paris 1830; Cyclopedia of Practical Medicine, Vol. III., article "Prognosis" by Edward Ash, London 1834; a unique article "On Prognosis," by William Farr, in the British Medical Almanack, 1839; "Observations of Prognosis" Vol. XLIV, Guy's Hospital Report 1887, P. H. Pye-Smith, and another article by Pye-Smith: "Observations upon Certain Elements in General Prognosis, upon the Particular Prognosis of Phthisis and of Enteric Fever." An oration on Prognostics was delivered before the Hunterian Society of London in 1858 by Doctor Munk, from which the following is quoted to add the valuable included historic data:—

"Coincidently with the return from the polluted stream of Arabian Medicine to the pure fountain of Grecian physic, was the renewed cultivation of a rational and scientific prognosis. It was in connection with a humoral pathology that prognosis made the greatest progress and achieved its highest triumphs."....."The doctrines of solidism on the other hand have uniformly proved inimical to the study of prognosis"..... "Prognosis was but little regarded by Hoffman, and still less by Cullen. To the neglect it experienced from the luminary of the Edinburgh School, its decadence in this country (England) is to be attributed. The pupils of Boerhaave and of the school over which this name and example continued to shed luster, were still cultivating prognosis in all its minutiae,

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and applying its rules with startling accuracy at the very time when Cullen's genius blazed above the medical horizon; and it was not until these had died off, and Edinburgh had taken that place in public estimation as a medical school, which Leyden had previously enjoyed, that the regular minute and systematic study of a rational prognosis became extinct in this country."

Dyce Duckworth in the paragraph following the above which he also quotes, writes: "I think that just consideration of the prevailing doctrines of pathology at the present time may encourage us to hope that renewed attention and study may henceforth be directed to the subject of prognostics."

Reynolds in his System of Medicine in 1866 declared "the practical test of a true science is the power which it confers of 'prevision' or knowing what will follow hereafter."....."When we can prognosticate with certainty, medicine will have become a science"....."Life is too subtle for us to know or measure all its possible contingencies."

The more recent English publications include the classic contributions of Sir Dyce Duckworth (London 1896)—from whom, for these General Considerations I have gained many facts; the oration of George Dock on "Prognosis, Its Theory and Practice" (The Journal of the American Medical Association, 1904). In German, Franke's "Lehre von der Bedeutung des Pulses und die Respirations Frequenz für die Prognose acuter fieberhafter Krankheiten" (Beitr. z. Pathol. u. Physiol., Berlin, 1878, III., p. 303) remains a classic in medical literature. They also include C. Gerhardt's "Ueber Vorhersage am Krankenbette (Münch. Med. Wochenschr., Nov. 24, 1896); the contribution of Moritz E., "Ueber Lebens Prognose," 1905; an article by Neuburger, "Zur Entwicklungsgeschichte der Prognostik" (Wiener Med. Presse, 1907); and the brochure of Norbert Ortner on "Klinische Prognose," Wien, 1908. Short, in England, with the assistance of over twenty clinicians has edited an Index of Prognosis which includes surgical affections (London and New York, 1915).

The eloquent Address in Medicine, on Medical Prognosis, delivered by Chauffard at the Seventeenth International Congress of Medicine (London 1913) has awakened anew the interest in the Presage of Disease. Chauffard clearly demonstrated that the paths to prognosis are open by the study of morbid disturbances, and by the "analytical method with the help of a more and more penetrating technique."

For safe prognosis we assume that pathology is but perverted or, as Chauffard says, "deviated" physiology, and disease, a disturbance of normal functions. We must associate with our knowledge of pathology a thorough acquaintance with the resulting functional disturbances. But while we gauge the result of disease on the various functions of disturbed organs there are innumerable factors which influence the prognosis of disease.

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Exogenous and endogenous influences must be considered.

The defensive reaction of the blood and the cellular elements to bacterial contamination and mechanical insult, the prompt alignment of the protective forces against the invading army, become at once factors with which the prognostician must reckon.

There are factors of which we are still uncertain which lead to the *formation of antibodies, stimulate cellular elements to activity and increase, provide the blood with opsonins and other protective substances, produce protective exudates, stimulate organs to compensatory action, promptly arouse the innumerable "factors of safety"* which are present in almost all of our organs (Meltzer), and *light to activity that innate, indefinable resistance which is so prominent in some and so feeble in others—all of which are potent factors for rational prognosis.*

The influence of *age* is always important. Experience teaches how variable this is in different diseases. Diseases which are well borne by the young are often promptly fatal in the adult and in the aged. Thus diabetes is uniformly fatal during early life, often without serious consequences after the thirtieth year; pneumonia and typhoid fever on the other hand show a reversal of this prognosis; endocarditis following or associated with rheumatism in the young is always ominous; in the adult it is less serious; arteriosclerosis is among the conditions which are fatal during early life; the aged may live on with advanced arterial change with but few or no symptoms.

An element which often influences prognosis unfavorably is the *tolerance of organs to pathologic change during long periods, without revolt.*

Early diagnosis improves the prognosis of most diseases.

The tolerance of the stomach, intestines and other organs during long periods to invading cancer or other organic diseases without subjective manifestations brings the victim to the physician long after the initial period of the disease. The gradual unobserved advance of arteriosclerosis with kidney invasion is another example of insidiously increasing and unrecognized, but serious, disease.

The *localization of lesions* is another factor which influences prognosis materially. The same general pathologic change so localized as to allow continuance of function practically unchanged, offers a more favorable prognosis than does a similar deposit so localized as to interfere at once with the necessary productive power of the organ.

The *influence of occupation* in inviting disease and in fighting it is among the important questions to be considered in connection with prognostics.

The *increase of cardiovascular lesions dependent upon changed social and business conditions,* the alarming arterial breakdown in men and women in the professions, especially the medical, the increase of cancerous diseases with advancing civilization, are among the problems which demand

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serious thought and attention in the attitude of the clinician to the individual and to the public.

The *influences of "constitution"* and the *"diatheses"* on prognosis, particularly during early life, are paramount. The inherent *endogenous factors* which so *change the blood plasma* of children burdened by diathesis remain unexplained; they exist and handicap the child in the race of life. The knowledge of the presence of such condition makes it possible for the parent, aided by the attendant, to supply the resistance which in many instances proves sufficient to bridge the child over critical periods.

The resistance which the different races offer to disease is among the interesting studies connected with prognosis, as well as the *immunity which certain sections enjoy.* Thus there is a decided variation in the *vulnerability between the light and dark complexioned races.* Dyce Duckworth says: "The vital resistance and *invulnerability of the Hebrew race* is, to my mind, very noteworthy. So much so is this the case, that I am wont to frame a better prognosis generally for Jewish patients under all circumstances." In spite of this fact *diabetes mellitus is most prevalent among the Jewish race.*

The negro invites *tuberculosis and smallpox,* and in him, both diseases are surprisingly fatal.

The influence of habits, alcohol and intemperance, early training, exercise, exposure, environment, social status and the innumerable factors which arise in individual cases under the many conditions of life, each demands special consideration and proves the complex nature of prognosis.

The varying character of epidemics, malignant during one outbreak, benign in another; the milder character of the cases toward the end of epidemics, the seasonal influences, *the variation in the virulence of the separate strains of infecting organisms, the immunity to infection against certain disease-producing germs* which often exists in the individual, *the differences in disease to leave permanent immunity after a single infection* and the *predisposition to repeated infections with a like offender,* often remain without satisfactory explanation, but all have a direct bearing on prognosis.

There are facts which influence the acute infections, with which it is always safest to remember the admonition of Hippocrates: "In acute disease it is not safe to prognosticate either death or recovery."

It is equally important for the conscientious clinician to consider the *fate of the descendants of his patients as well as their antecedents* (family history). The application in practice of the *Laws of Heredity* demonstrated by the *teachings of Mendel* and his followers will prevent untold misery to many, during many generations. The improving of the "racial qualities" as advocated by the modern science of Eugenics cannot be accomplished without the coöperation of the clinician.

The questions connected with prognosis include the *after effects of dis-*

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ease as well as the relations of the infected individual to his surroundings. The prognostics of the infections teach the urgent need of *long surveillance* of the individual patient and the recognition of the *dangers to vital organs after acute disease.* This is particularly true of rheumatism, scarlet fever, pneumonia, typhoid fever, influenza and the exanthemata.

The infected individual relieved of his acute symptoms may still be dangerous as a "carrier" and often becomes the starting point of far-reaching disease.

The *milder infections are as dangerous to their surroundings as are the more malignant and should be so considered by the proper authorities.*

The influence of *neurophathic tendencies and the traumatic neuroses* on prognosis is not to be lightly regarded. What Sir James Paget so happily named *"the Mimicry of Disease"* includes a chapter in medicine (*Neuromimesis*), which for its full interpretation and prognostic significance requires enormous knowledge, tact, and a judicial mind. The underlying anomalies leading to the complex of *Neurasthenia* may be said to include the same requirements for reliable prognosis and its rational treatment as the Neuromimeses.

Phagocytosis and extra cellular digestive processes are elements of enormous value in prognosis. The cure of bacterial disease results from the destruction of the micro-organism in the organ invaded and in the blood, by the aid of phagocytosis and the activity of extra cellular digestion.

Hoekten has demonstrated in pneumonia—and this is probably true of other infectious disease—the general defensive reactions of leukocytes and the production of antibodies "of which the opsonins are the best known." *With inadequate destruction of pathogenic bacteria in individual disease and their proliferation, with the absence of antibodies from the blood the prognosis is bad; there is no army to meet the invading forces.*

The influence of acute infections on existing chronic diseases is often overlooked, faultily interpreted or not considered at all in framing the prognosis. The favorable influence of acute infection on the course of chronic disease at times has been fully appreciated, and the literature of the subject contains a number of striking examples taken from the experiences of acute clinical observers. In occasional cases chronic processes of long duration have been so favorably influenced as to disappear entirely. In some the disease is held in abeyance only during a limited period, while in other cases the clinical picture of the disease may be materially changed by the added infection.

Gerhardt reports:

I. Trigeminal neuralgia relieved during acute pneumonia.

II. Tuberculous ascites has after profuse diuresis been relieved during croupous pneumonia.

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III. Chronic arthritis—so-called rheumatism—has been without symptoms during acute tonsillitis.
IV. Acute psychosis is often controlled during erysipelas.
V. Measles has relieved the pressure symptoms of brain tumor.
VI. Chronic malignant tumors, facial carcinomata (epitheliomata) have often shown marked improvement, even cure, after erysipelatous infection.

Kopff has seen subacute arthritis promptly cured spontaneously by erysipelatous complication.

Measles has cured eczema capitis, chronic pemphigus, chorea, epilepsy and urinary incontinence.

One infection grafted on another is likely to influence the primary infection. Splenic fever is prevented experimentally by inoculation with the erysipelatous streptococcus, prodigiosis, staphylococci or the Friedlander germ. The influence of pneumothorax on the chronic tuberculous lung disease is thoroughly recognized.

Naunyn has observed the favorable influence on sugar loss, without increase of hyperglycemia with the intercurrent infections of diabetics.

There are cases of pernicious anemia which with tuberculous infection show an improved blood picture (Diabella).

The influence of tuberculous disease on the leukemias, also other infections, is often striking and favorable (See Leukemia for Elsner and Groat, also Dock's references).

Collective investigation of disease has resulted in the accumulation of data which strengthen prognosis and make it more certain than ever before. Among the diseases thus studied are tuberculosis, typhoid fever, the results of inoculation against the latter and against smallpox and diphtheria. The collective data which prove the prognostic value of the recognition of the specific nature of many *brain tumors* and the *dependence of many liver enlargements and diseases on syphilis*, and their disappearance under specific treatment are noteworthy. The subject of *Cretinism* and its prognosis has been enormously advanced by the collective investigation made in England. A basis for classification was given and the influence of the organic extracts—the introduction of which is easily the most marvelous advance made in medicine during the past century. The prognostic significance of the general symptoms (pulse, respiration, fever, et cetera) will be considered with the separate diseases.

Tact and humanity combined, with all that is complete and highest in our art, a full knowledge of all that makes the cause and recognition of disease possible, scientific methods of treatment with reasoning ability sharpened by well digested experience and a delicate poise, are among the requirements necessary for prognosis.

The question often arises in the course of practice whether it is wise

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to give an unfavorable prognosis in the individual case. *The tactful physician will rarely do harm to his patient by leading him to an appreciation of his condition without robbing him entirely of the hope to which he is entitled. The element of Hope in prognosis ought never to be disregarded.* It means much to be aided by a suggestion which stimulates hope. In cases of positively fatal diseases this will occasionally prolong life; if it does not do this, it certainly adds materially to the comfort of the individual and makes pain and mental pang more bearable. The power which the experienced physician holds over the patient for good or ill, by giving thoroughly considered and honest prognosis, is enormous. Much depends upon the method and tact of the attendant.

Patients with acute infectious diseases rarely inquire *themselves* as to the outcome; those afflicted with sub-acute or chronic ailments unless they are deluded and fail to appreciate the seriousness of their maladies are eager for an honest prognosis. I have always contended that *either the patient, some interested member of his family or close friend is entitled to such information concerning the course of the disease as the physician can give with reasonable certainty. Distortion and misunderstanding cannot always be prevented.* Where prognosis is impossible in the presence of a large element of uncertainty, the ignorant as well as the intelligent will respect the physician more for having candidly and without equivocation given expression to an opinion which proves his limitations than to a prognosis which finally proved to be incorrect. Patients when properly informed are led to a thorough appreciation of the gravity of their condition, but also understand that the physician is not infallible and that in the end Nature may come to the rescue. Further, the tactful physician, with patients even of ordinary intelligence, can so frame his prognosis without injury, as to lead to the peace of mind which follows attention to the requirements of religion and to material affairs. In my experience I have invariably among our Catholic patients in hospital and in private practice given ample time for the administration of the rites of the church in all cases where life seemed threatened by disease, usually with comfort resulting, without unfavorable influence on the course of the disease; in many cases the fight has been renewed and won.

Cruel and heartless prognoses which rob the patient of all hope are never justified; one can be truthful without being barbarous.

Thoughtless and unqualified prognoses have often led to sudden death and suicide. The blunt and inconsiderate prognosis of ultimate blindness in a case of locomotor ataxia in one of our patients made by a busy, thoughtless ophthalmologist after a single examination of the background of the eye, without a knowledge of the previous history of the case of long continued eye symptoms, was followed by the suicide of the patient within the following twenty-four hours.

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The physician in many cases needs to be guarded lest he betray his feelings during the examination of the patient before he has thoroughly assimilated the facts in the case sufficient to lead to a diagnosis.

Gardner says "Beware the unguarded word! Beware the unguarded hesitation! Beware even the unconscious sigh."

The *setting of a time limit in framing prognosis is indiscreet, unsafe, unscientific.* The physician may guess right and thus strengthen himself in the minds of the ignorant, but to the thinking layman and to the scientific, such a forecast is without value and weakens faith in the profession.

Optimism in prognosis whenever honestly possible is justified. "It is not only the privilege of the physician but his bounden duty" to continue hopeful, for it may turn the scale in favor of the patient and start him toward recovery. Unwarranted optimism, however well intended, may lead to embarrassment and should not be encouraged.

Honest suggestion with prognosis is an asset which belongs to the physician's armamentarium. Though we may not always be justified in giving hope of complete cure, partial relief in many cases may be predicted. We are often certain that the underlying pathologic condition can never be removed, but life may be prolonged and usefulness continued. Percival's advice in this connection is wholesome. "A physician should not be forward to make gloomy prognostications, because they savor of empiricism, by magnifying the importance of his service in the treatment or cure of disease." . . . He should "give to the friends of the patient timely warning of danger, when it really occurs and even to the patient himself, if absolutely necessary."

Not infrequently we are for a time, unless on guard, misled to change an original diagnosis and discredit prognosis. This is often true in cases of *pernicious anemia,* when for a time the disease remains stationary or improvement continues during long periods; in cases of *ulcer of the stomach and duodenum,* when symptoms disappear, but finally recur; in *leukemia,* in which modern methods of treatment lead to surprising but *temporary reduction of lymphocytosis;* in cases of *cancer,* where during long *periods of latency* the clinical features are entirely changed.

In early life, we know the baneful influence of tuberculous glands; long periods of health may follow their neglect but in the end the original prognosis must stand.

So, too, we are justified in calling attention to the *grave import of the neglect of treatment* of many diseases, in spite of few or annoying subjective or objective symtoms.

The early diagnosis correctly made must always remain the foundation of authentic prognosis.

The physician as his experience grows reaches conclusions which modify prognosis from his *general survey of the patient,* exclusive often of

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physical signs and subjective complaints. The *physiognomy, the facies of the patient, the expression, the brilliancy or dullness of the eye, the way in which the patient lies or handles himself in the midst of serious disease, more particularly the infections; it is in short the picture which allows of no description, which cannot be defined, which impresses the clinician and materially influences the forecast.* Dyce Duckworth has well said: "The organs may be found in detail free from structural disease, but there may be appearances and features indicative of progressive failure not yet registrable by the stethoscope or the test tube, of which the significance is of the last importance, and these may escape recognition and appraisement. . . . A little more attention to the individual, his aspect, his gait, and his manner, would sometimes be well repaid in a sounder appreciation of his life value. . . . I am constantly training students to begin by looking at their patients." We often fail to take the time "for a meditative survey" of facts in order "adequately to apprehend the general laws which underly and govern them." (Duckworth.)

All of these facts prove that *the art of prognosis can never be acquired from books.* The clinician will rarely fail if he has the ability to read disease, if he correctly appreciates that added to his scientific knowledge, gained after painstaking examination and investigation, divorced from the test tube and the microscope, there is much which the ready eye sees which must influence him in treatment and in prognosis. Sir Jonathan Hutchinson was profoundly impressed by the lectures and clinical teachings of Laycock, afterwards Professor of Medicine in Edinburgh, for he taught the "value of the general appearance of physiognomy of the patient as an indication of his physical condition."

"An entirely modern idea—but one which should imbue our minds nowadays—is that of defining in each particular case the mutual relationship between those three fundamental elements of medical judgment; *to know, to foresee, to act.*" (Chauffard.)

"As observation becomes more accurate, as the number of observed cases increases, and as classes are better and better distinguished, the nearer will the physician be able to approach an accurate prognosis, though the time when any sufficient rule can be applied to individual cases must long be out of our sight and the application of any approximate rules must long be subordinate to the instinctive tact of the educated physician himself, who alone can apprehend the sum of the peculiarities which must modify their application to individual instances" (Allbutt).

With this statement before us, mindful of the many perplexing problems included in Medical Prognostics, I hesitated to present any material to the profession until I had a long and broad experience in both private and hospital practice.

I have sought in the consideration of the separate diseases to consider the cause and nature of the pathologic processes in connection with symp-

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toms and signs and to add to these my knowledge of the outcome of the combinations in the series of cases which served to supply the material.

As I said in the preface, my desire is to bring comfort to the physician, and through him benefit to the patient; this I expect to do by stimulating the study of the forecast of disease through pathologic knowledge, diagnosis—as accurate as it can be made in the present state of our knowledge—with tact and humanity.

"He who remains silent will not easily err. He will never shoot at a target, will therefore never miss it, but he will never be a thorough marksman" (Gerhardt).

We will often be disappointed and uncertain, "but since the science of prognosis is one of the loftiest summits of medicine" (Chauffard) we are never to slacken our pace. To make the supreme effort is our duty than which there is no greater stimulus to the active physician.

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Section I

Specific Infectious Diseases

A. Protozoan Infections

I. Syphilis

Lues

Syphilis is a specific disease due to the *Treponema pallidum* of Schaudinn (1905), which invades the blood and all tissues of the body from the primary and local lesion—the latter characterized by ulceration and inflammation at the seat of inoculation—with prompt lymphatic invasion, probably a rapid, possibly a single excursion of the Treponema through the blood-stream to the various organs of the body, in which, after longer or shorter periods local changes of a productive and destructive nature may follow, depending on many factors, the most important of which is the early and intensive treatment of the disease.

Wassermann Reaction.—Syphilis is inoculable to the ape and offers a positive Wassermann reaction which includes the indirect recognition of a specific antibody by the fixation of complement test. In the carrying out of the test through its two stages in the tubes in which complement has been absorbed, hemolysis is absent, therefore the test is "positive"; in the tube in which there is hemolysis the complement has not been absorbed and therefore the test gives a "negative" result.

The Wassermann reaction is so exceptionally present in non-syphilitic diseases that its presence in suspected syphilis justifies a positive conclusion.

The few diseases in which the Wassermann reaction is present offer such positive symptoms as to make differentiation easy. Included among these are *leprosy, frambesia, scarlet fever*, rarely; occasionally *cancer, tuberculosis and pregnancy complicated with acute yellow atrophy of the liver* (Scholtz).

We consider the prognosis of syphilis based upon the following classification:

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1. Acquired Syphilis.
   (a) Early manifestations.
      (i) Primary and secondary stages.
   (b) Late manifestations.
      (i) Tertiary stage (including visceral syphilis.
      (ii) Late tertiary lesions — so-called metasyphilitic lesions.
2. Congenital Syphilis.
   (i) Intra-uterine.
   (ii) Post embryonic.

Acquired Syphilis

With the introduction into medicine by Ehrlich of chemotherapeusis including salvarsan, neosalvarsan and its modifications, the prognosis of all forms of syphilis in all of its stages has been enormously influenced, though we must confess that long years of observation are needed before positive conclusions can be reached which justify a forecast of the syphilitic's future who to-day subjects himself to the modern and supposedly rational treatment of the disease.

By modern diagnostic methods, i. e., the Wassermann reaction and the examination of the spinal fluid, we are able to reach positive conclusions with regard to the activity of the infection in all of its stages.

Primary Stage

During the primary stage of the disease the patient as well as the attendant should recognize in syphilis a serious infection, which, if a favorable forecast is to be given must include not the treatment of the palpable and visible symptoms alone, but the constitutional invasion by intensive methods. The prognosis of untreated cases of syphilis is unfavorable for the subject infected, his offspring, and for the nation. There is no spontaneous cure of syphilis; no subject is safe to his surroundings who has remained untreated. Symptoms may disappear during periods which vary in length, but in all there are recurrences which include detected or undetected lesions (mucous patches especially) from which infection may spread to the innocent. Bramwell has called attention to the fact, and his experience is corroborated by that of others, that those syphilitics are most likely to develop the serious late manifestations of the disease who are insufficiently treated during the primary and secondary stages; who, after the disappearance of visible lesions neglect themselves. *The prognosis, therefore, of constitutional syphilis is enormously influenced by the rational, scientific, and intensive treatment of the early manifestations of the disease.*

Not all subjects react alike to syphilitic infection. In some, we find a

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tendency toward malignancy in the obstinacy of the initial lesion and in its *early tendency to deep destructive changes* with *marked constitutional disturbances;* and in some, the *early invasion of the nervous system.* Others, present features which at once brand the infection, so far as evident changes and reactions are concerned, as benign during the early days of the disease. Such behavior should not mislead, for mild and evidently benign cases during the early stage may offer late manifestations and so-called metasyphilitic lesions out of all proportion to the benign nature of the early symptoms.

Syphilitics who are reduced by PREVIOUS DISEASE, constitutional anomalies, who are inherently weak and nonresistant, are likely to show the effect of such handicap during the early stages of the disease.

The influence of syphilis on tuberculous disease is considered separately (See Tuberculosis).

ALCOHOLICS and the DISSIPATED are prone to show ulcerative and destructive changes, with marked constitutional disturbance during the primary stage of the disease. The phagedenic tendencies of syphilitic tissue in alcoholics is characteristic.

The AGED AND OVERWORKED who contract syphilis show great tendency to destructive and constitutional symptoms, including wasting of tissues, anemia and asthenia.

Blood Changes During the Early Stages.—Marked changes in the RED CORPUSCLES during the early stages are exceptional. There may be a slight reduction of erythrocytes, but this is not significant.

In the exceptional case in which there is a material reduction of erythrocytes—late during the primary and in the secondary stages—the infection is severe, or there is lowered vitality of the patient, previous disease, or some one of the diatheses.

The HEMOGLOBIN during the secondary stage in the average case which progresses favorably does not fall below 70 per cent, while as Naegeli has shown, the red blood-corpuscle reduction is insignficant.

When during the secondary stage hemoglobin falls to 30 per cent or only slightly higher, the infection is severe and the prognosis should be guardedly given.

Several authors have claimed that there is a lymphocitic increase during the acute stage; this we have not been able to confirm. It is safe to conclude that the lymphocytes are markedly increased only when the patient shows marked improvement after the early stages and as Naegeli reports, this should be regarded as a "'post-infectious lymphocytosis." High leukocytic counts are rare (24,000). Our average leukocytic count of the secondary stage is between 9,000 and 11,000. With leukocytosis, if present, the large mononuclears are increased. Following the injection of salvarsan, with the improvement of symptoms, a slight increase of neutrophils is found without the disappearance of eosinophils.

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Constitutional Symptoms.—During the primary stage there are rarely threatening or even serious constitutional symptoms from which the subsequent course of the disease can be foretold.

The *fever of invasion* may be associated with constitutional disturbances including malaise, rapid pulse, depression and myalgia; the fever may be markedly intermittent, remittent or during a limited period may remain continuous, thus clouding the diagnosis.

With all syphilitic febrile anomalies, the prognosis is good and convalescence rapid.

Wassermann Reaction During the Primary Stage.—Positive Wassermann reactions are not present during the early days of the initial lesion.

In 70 per cent of cases, the reaction is positive between the fourth and seventh week.

The time of constitutional invasion corresponds with the appearance of the positive Wassermann reaction. Bayly says: "Primary cases in which the lesion has been present for less than a fortnight almost invariably give a negative reaction, while 75 per cent of positive reactions are obtained if the primary sore has been present for over a month."

Secondary Stage

The secondary stage is reached in from four weeks to three months after the appearance of the initial lesion.

While the lesions of the secondary stage may be numerous, there are rarely serious complications during this stage.

Positive Wassermann reaction is present in practically all cases during the secondary stage of the disease, showing itself between the fourth and seventh week after the appearance of the initial lesion, as already mentioned (95 to 98 per cent). The Wassermann reaction is also positive in 90 to 95 per cent of cases during the tertiary stage (Scholtz).

Skin Lesions During Secondary Stage.—The *roseola eruption* may be so slight as to escape detection; with modern treatment it is usually absent. It is not persistent, and fades entirely in from four to fourteen days.

Papular and pustular eruptions are more persistent than is the roseola syphilitica.

Early pustulation in our experience has been evidence of the most rebellious type of the disease. *Squamous syphilids,* early, are also evidences of resistance to the treatment, and unless they yield after systematic and intensive treatment, may be considered expressive of the more malignant types of syphilis.

But few cases escape *mucous patches*: in all cases they are likely to recur. Their presence is always positive evidence of active syphilis and we place great importance upon this lesion in framing the prognosis which includes indication for the future treatment, and in deciding the many

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questions associated with modern eugenics. We insist that *the presence of the mucous patch, wherever found, should lead to further observation and intensive treatment and always argues against the advisability of marriage.*

The prognosis of syphilis during this and subsequent stages is unfavorably influenced by the neglect of treatment: to wait until secondary symptoms appear is unwarranted, and influences the case unfavorably.

The negative Wassermann reaction during the early stages of syphilis does not justify the conclusion that the syphilitic is cured. The negative phase may be followed by a positive reaction and a return of symptoms.

With lesions suspicious of the secondary stage, mild or incomplete reactions should not be accepted as conclusive evidence, and should lead to further tests.

The *fever of the secondary stage* behaves much like that of the primary; there may be no fever during the latter stage, or as usually happens, the fever begins with the end of the primary and the beginning of the secondary stage. In all of these the prognosis remains unaffected. The majority of cases remain afebrile throughout the early stages, or if fever is present, patients fail to recognize it.

Accompanying Manifestations.—The severity and localization of the lesions of the secondary stage depend upon the seat and extent of the deposits of the Treponema. The excursion of the Treponema pallidum through the blood is immediately followed by its deposit in the various organs of the body. The skin receives the larger number of spirochetes; hence the multiplicity and preponderance of lesions in it. The treponemata are held in the contracted capillaries of the skin, where they proliferate and cause changes.

Alopecia.—Pronounced alopecia is evident in many cases; few that are radically treated have more than insignificant loss of hair. It is relieved quicker than is leukoderma; it rarely causes permanent bald spots (alopecia areata). Alopecia is, in most cases, favorably influenced by radical treatment.

The other skin lesions of the secondary stage including the small papular syphilid, leukoderma, serpiginous and psoriatic syphilids, and condylomata are all amenable to treatment.

Condylomata.—Condylomata are a source of infection and should be so regarded by the clinician.

Nephritis.—Nephritis sometimes develops during the secondary stage. The prognosis will be considered with the visceral lesions of the tertiary stage of the disease.

Arteritis.—Arteritis may be an early complication; it may invade the cerebral, renal, or coronary arteries or may be general: the prognosis is not bad if detected early.

Early Myocarditis.—Early myocarditis may prove threatening; its

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rational treatment usually leads to recovery. It will be considered under Heart Complications with visceral syphilis.

Joint Invasion of Secondary Stage.—The joint invasion of the secondary stage is not serious. There is improvement under treatment after a few days or weeks of ill-defined pain, which may resemble acute or subacute arthritis, occasionally gout—without recurrence in most cases.

The Eye.—Inflammatory conditions of the eye are not uncommon; the most painful and threatening among these is *iritis*. This usually yields to treatment after several weeks; there is but small remnant of disease left. In some cases adhesions cause permanent damage, though sight is preserved and often somewhat reduced.

The Ear.—Ear changes are rare, when present they yield slowly to treatment.

Lues Maligna.—The evidences of malignant lues during the early stages include ulceration of the skin and mucous membranes which may be disseminated.

Papular lesions may promptly ulcerate; ecthymatous lesions are also characteristic with the development of *rupia syphilitica*.

These lesions of malignant lues during the secondary stage do not develop, as do the ulcerations of the tertiary stage from gummatous tissue, but from the small and rapidly ulcerating papule or pustule. The fate of these, in the malignant cases of secondary syphilis, is surprising rapidity of ulceration with the upbuilding of crusts and the characteristic lesions of ulceration, the edge of which is in direct contact with the normal skin.

"Galloping syphilis," "malignant" and "florid," always gives a positive Wassermann. Galloping syphilis is associated with marked constitutional disturbances, high fever, rapid pulse, and early arterial degeneration of an amyloid character. The prognosis of these cases in spite of active treatment is often bad. Many of these malignant cases bear medication badly; and when they do improve relapses are frequent and threatening.

Evidently the subjects of malignant lues, for some reason, have less resistance to syphilitic infection than is possessed by average normal individuals (Scholtz). Finger believes that in the ancestors of these subjects syphilitic infection was absent during many generations and because of the lack of the average immunity caused by such infection, the malignancy corresponds with that of the disease during the early years of its existence in Europe. The absence of marked enlargement of the lymphatic glands during the early days of syphilitic infection in malignant cases, and the consequent failure to get the protecting influence of these, is advanced by others as a cause for malignancy.

In some of the malignant and galloping cases, cachexia, diatheses, previous disease and dissipation, should be considered as provocative. *Malignant lues, complicated with visceral lesions early, offers a very dubious prognosis.*

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Period of Latency.—This period has been described by Browning and Mackenzie as "a state of equilibrium between the host and the parasite" (Bayly), while Ehrlich gave it the name of "non-sterilizing immunity." In the majority of cases, following the symptoms of the secondary stage as shown by skin lesions, mucous patches, and the positive Wassermann reactions, all symptoms may disappear and to all appearances the subject is cured; in 50 per cent the Wassermann reaction becomes negative. For safe prognosis, these cases should be considered to be in a latent stage, and a positive forecast should not be offered. Relapse from the latent stage is the rule in from three to nine months with either mucous patches—usually buccal or tonsillar—skin lesions, and the return to the positive phase (Wassermann) of all.

The foregoing facts are of enormous prognostic significance and their correct interpretation means much to the patient and his surroundings. *The great value of the Wassermann reaction for the indications which it offers for treatment and prognosis* must be recognized during this stage; it discloses "these hidden or latent cases, and in this way to cure them and to protect against the much dreaded parasyphilitic complications" (Neisser). The lighting of the disease to activity, as is shown by the return of the positive Wassermann reaction, where before the blood gave a negative response and an increase in the depth of color of existing skin lesions, is known as the *"Jarisch-Herxheimer reaction."*

The prognosis of these cases is enormously improved for the recrudescence of the infection, and further lesions are prevented by appropriate treatment and the following of the indications offered by repeated Wassermann reactions. In some, the latent phase is promptly changed to a positive reaction by the treatment. We quote from Bayly: "A single negative reaction obtained with the serum of a patient undergoing treatment by mercury or salvarsan means little but that the patient is reacting to such treatment. A series of negative results taken at intervals of three to six months after all treatment has been given up is necessary before the patient can be regarded as cured, and even then, until twenty years have passed, we cannot be absolutely certain that the disease is completely and permanently obliterated and that no late manifestations will ever occur. It is most important to remember that about 10 per cent of untreated cases of syphilis fail to give a positive reaction at the first examination, and that therefore a negative reaction only gives a 90 per cent probability of freedom from infection."

During the secondary stage of the disease, the influence of the treatment on the Wassermann reaction offers decided indications for prognosis and the modification of the further treatment. If with treatment the reaction continues strongly positive, the medication is insufficient and the disease uncontrolled. If the Wassermann reaction (a smaller complement is fixed) shows decided change, feeble reaction or the negative phase, the

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treatment is efficacious—the disease is under control and the prognosis is correspondingly better.

Length of Secondary Stage.—The length of the secondary stage is variable. It may cover a long period of years, rarely longer than 4 to 5 years, though mucous patches and small and large papular syphilids are found long years after the clinician had considered the stage passed. *Smokers* may show mucous patches so long as twenty and thirty years after infection. It is impossible in the individual case to be positive that the secondary stage is ended, until symptoms of the tertiary stage develop. This is an important fact. The secondary stage continues to be dangerous because during its persistence the disease continues communicable.

The Cerebrospinal Fluid.—The lumbar fluid gives valuable data for prognosis in the advanced stages of syphilis and in the secondary stage. Dreyfus, who has now made over 1,500 lumbar punctures, finds a positive Wassermann reaction during the early stages of syphilis in over 80 per cent of all syphilitics. This proves the early dissemination of the Treponema to the central nervous system, and that this may exist without subjective symptoms. It is assumed that a persistence of the Wassermann reaction during and following the secondary stage—a condition which is usually due to faulty treatment or malignancy of the infection—makes the prognosis unfavorable; for such subjects will be likely to develop serious nervous lesions: they are candidates for late tertiary disease (paresis, tabes, etc.) Under improving conditions during the early stages—usually due to treatment and rational living—the previously increased intralumbar pressure is lowered, the Wassermann reaction becomes negative in the blood and in the lumbar fluid.

The influence of treatment on prognosis during the secondary stage can be best interpreted by the results of the Wassermann test of the blood and the lumbar fluid. Positive Wassermann reaction of the lumbar fluid in the secondary as well as in all stages of syphilis must be interpreted as positive evidence of specific infection of the nervous system, and until a negative phase is reached the disease cannot be considered to be under control; hence the enormous influence on prognosis of these results. We will refer to the importance of the examination of the cerebrospinal fluid in connection with late tertiary disease. The blood may give positive Wassermann reaction, but unless the nervous system is involved, the spinal fluid will continue to give negative results. Besides *increased pressure* there is marked *increase of albumin* during the secondary stage; both disappear under proper treatment. During this stage there is marked *lymphocytosis* of the fluid, and with severe nervous symptoms this is decided with great increase of the albumin content. Lymphocytosis of the fluid attends over 50 per cent of all secondary syphilis. Plaut claims that the cerebrospinal fluid shows *leukocytosis* in one-third of all secondary syphilis, one-third are on the border line, and the remnant shows no cellular increase."

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Tertiary Stage

The tertiary stage of syphilis begins the period of late manifestations, during which there is no danger of infection to others, in which there may be years of latency, and in which visceral lesions may develop in vital organs. Tertiary syphilis, when it attacks the skin, leaves the remnant of the lesion which caused tissue breakdown in a characteristic cicatrix—in contradistinction to the secondary lesion. The cutaneous lesions are not so extensive as during the earlier stages, but more destructive. They are often asymmetrical, and during this stage, the internal organs may be invaded. The tertiary stage is characterized by the deposition of *gummata,* true *granulation tumors.*

The tendency of all gummata wherever found is to necrosis and cicatrization. Gummata vary from microscopic-sized to large orange-sized tumors—occasionally even larger.

The fate of the gumma of the skin is necrosis with ulceration, unless promptly influenced by treatment whereby these changes may be modified. When thus influenced, resorption takes place with resulting stellate cicatrization. In the liver, healed gummata often leave large and deep cicatrices with sufficient remnant of normal tissue to lead to unchanged function of the organ. We will refer to the behavior of multiple gummatous deposit and its prognostic importance in connection with a consideration of the separate organs involved.

Cutaneous Lesions of Tertiary Stage.—The cutaneous lesions of the tertiary stage include: (a) Papular syphilids (b) Gummatous syphilids.

(a) Papular Syphilids—Papular syphilids include tubercular, tuberculo-serpiginous syphilids, ulcerative serpiginous syphilids, rupia syphilitica and psoriasis syphilitica. In all of these, ulceration and cicatrization of the invaded tissue follow as a rule.

(b) Gummatous Syphilids.—It is difficult to draw a sharp line between papular syphilids and skin gummata; both rest on the same pathologic foundation. This is particularly true of the serpiginous syphilids which ulcerate (serpigino-ulcerative syphilids). Both forms of tertiary cutaneous syphilids offer a good prognosis in cases which are not malignant and which are subjected to rational treatment.

Neglected *gummata of the scalp* which invade the periosteum may lead to deep tissue loss and ulcerative destruction of bone.

Gummata of the nose, which are internal—invading bone and mucous membrane—lead to destruction of the septum and other changes. The result of bone destruction leads to the characteristic deformity known as *"saddle nose."* It often happens that gummata invade the nasal periosteum without causing symptoms sufficient to bring the patient to the physician, until irreparable injury has resulted. The perforation in such cases is the first evidence of destruction. The septum is the seat of gummatous deposit

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by predilection. The syphilids of the alæ nasi and other parts of the nose are often destructive in malignant and untreated cases: early prompt treatment, local and constitutional, usually leads to satisfactory results with little damage remaining.

Gummata of the tongue, soft palate, tonsils, and buccal mucosa tend toward prompt breakdown of tissue and perforation. Cicatrices often lead to adhesions and consequent distortion. The hard palate is often included in ulcerative destruction and is perforated.

The Blood during Tertiary Stage.—There is but slight, if any, change in the red blood corpuscle count; there may be slight anemia in the average case. *Severe anemias* are always an expression of malignancy—depleting conditions due to complications and cachexia. Almost all severe anemias occur during the tertiary stage of the disease; they may be of the chlorotic type without leukocytosis. With chlorosis there may be leukocytosis or an approach to the picture of pernicious anemia. It is very rare that death follows these severe anemias. The larger number are found in over-worried and weak women: many of these work and live in unfavorable surroundings.

Hemolysis following the administration of mercury may be a cause of grave anemia and is unfavorable; it shows intolerance of specific medication.

The presence of many *large mononuclear lymphocytes* has been reported by several reliable observers (14.1 per cent) (Hauck). The *leukocytic count,* in favorable and in the average cases, is between 9,000 and 13,000 (Sabrazes and Mathis).

Cerebrospinal Fluid during the Tertiary Stage.—In severe cases of tertiary syphilis the *albumin* content is large. *Leukocytosis* is found in cases which have been neglected or insufficiently treated. Disappearance of leukocytosis, and decrease of albumin, with lowered pressure, are proofs of improvement; there are exceptions to this rule, for occasionally the change is insignificant.

With involvement of the nervous system there is *lymphocytosis.* The cells are small mononuclear with a few larger kite-shaped lymphocytes; the nucleus is in the broadened protoplasm of the cell.

The presence of leukocytosis in the withdrawn fluid is always proof of organic disease, in spite of the absence of subjective symptoms. *Functional neuroses never show leukocytosis.* Lymphocytosis is proportionate to the gravity and extent of the inflammatory changes—usually in the meninges—and the prognosis can usually be favorably influenced by early rigorous treatment. Plaut, Bayly and others agree that a "negative cytological examination, namely, the presence of less than six cells per c. mm., will exclude general paralysis, syphilitic meningitis and tabes."

Frequency of Tertiary Lesions.—The frequency of tertiary lesions is certainly decreasing under modern methods of treatment and the increased

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knowledge of the effects of syphilitic infection among the masses. It is unfair to reach conclusions from hospital material alone, for such cases are usually found among the neglected, insufficiently treated, and the intemperate. Scholtz says that "the percentage may be placed between 15 and 20; more accurate statistics are not available, for the lesions of tertiary syphilis may not appear for twenty to thirty, yes, forty years after infection—periods so long that it is impossible to follow the cases and determine their fate."

Tertiary lesions are invited by depressing influences, alcoholism, faulty nourishment, diathesis, tuberculosis and lymphatism. Tertiary lesions are often present without the patient's knowledge of syphilitic infection: hidden, unobserved and untreated primary lesions account for these in over 50 per cent of cases. *But few, thoroughly treated during the initial and secondary stages of syphilis, develop tertiary lesions. Early and apparently benign symptoms do not preclude later malignancy and deep tertiary lesions.* Such cases are likely to be neglected; occasionally in spite of rational treatment they lead to so-called metasyphilitic disease. *Neisser's statistics* which follow, are of great value for our purposes: they show how rarely patients with tertiary symptoms are treated radically during the early stages of syphilis and how often patients with tertiary symptoms receive no treatment at all.

NEISSER'S STATISTICS ON TERTIARY SYPHILIS.

Tertiary Syphilitics Received.	Private Material.	Clinic and Policlinic, until end of 1893.	Clinic and Policlinic, 1894 and 1895.
No treatment, or treated but once insufficiently.	35.4 per cent. males 66.6 per cent. females	72.3 per cent males 80.45 per cent. females	68.8 per cent. males 76.8 per cent. females
But one cure.	23.3 per cent. males 16.5 per cent. females	20.4 per cent. males 14.25 per cent. females	14.0 per cent. males 16.0 per cent. females
Two or three separate cures.	29.3 per cent. males 8.5 per cent. females	3.5 per cent. males 2.4 per cent. females	8.9 per cent. males 5.8 per cent. females
Four or more (some thorough, others indifferently carried out) cures.	12.0 per cent. males 8.4 per cent. females	3.37 per cent. males 2.85 per cent. females	8.9 per cent. males 1.4 per cent. females

These statistics are corroborated by all experienced clinicians and syphilographers, including Fournier, Haslund, Ehlers, Neumann and Scholtz.

Visceral Syphilis in Tertiary Stage

The incidence of tertiary and metasyphilitic disease of the internal organs now considered late tertiary syphilis, has been proved by the newer

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methods of diagnosis—the Wassermann reaction particularly—to be more frequent than has been heretofore suspected. When we include among these the many cardiovascular conditions, formerly unexplained, and the specific diseases of the nervous system now known to be of luetic origin, we add an enormous material, and increase the percentage accordingly.

Visceral syphilis includes the diseases of the internal organs which develop during the tertiary stage of the infection. It must not be forgotten that occasionally vital organs are attacked during the secondary stage of the disease; these include the kidney, central nervous system, the osseous system, the vascular system and rarely the liver. The organs which are attacked during the tertiary stage include the arteries, veins, the heart, the liver, the kidney, the bones and joints, the rectum, the digestive tract, the spleen, the testicles, the bladder and genitalia, the respiratory organs, and the central and peripheral nervous system.

Specific Diseases of the Cardiovascular System

Arteritis.—The classic work of Heubner, in which he called attention to the importance of lesions of the smaller cerebral vessels, which are always characteristic of endarteritis, in which the intima is the seat of proliferative change—still serves as the basis of our knowledge of the subject. The disease does not limit its ravages to the intima, for in advanced specific arteritis all coats may be invaded. The student of medical literature is referred to Virchow's comprehensive treatment of visceral syphilis, which is one of the most marvelous additions of the past century.

It can be easily understood how far-reaching the influence of specific arteritis may be, and how many organs may suffer at the same time. Such weakening as is caused by endarteritis specifica of the arterial walls may lead to miliary or large-sized aneurysmal dilatation, with the included secondary manifestations. (Aneurysm of the aorta and larger vessels are separately considered.) The changes which follow in the cerebral vessels and their baneful results, with prognosis, are considered with Cerebral Syphilis.

With practically all specific arteritis the Wassermann reaction is positive. *Specific arteritis invading the coronaries* gives rise to threatening symptoms, including the complex of *angina pectoris.* It must be remembered that *stenocardia* is not always, even during early life, of specific origin. Heredity is an important factor in many; but in young subjects evidences of arteritis, including coronary invasion, should always lead to the strong suspicion of syphilis as a cause, to corroborative Wassermann tests, and specific treatment. If the myocardium is not too far degenerated, and other vital organs are not invaded—kidney, brain, etc.—the prognosis is fairly good.

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No specific arteritis is so far advanced as not to justify specific treatment, for in extreme cases we are often unexpectedly successful. Results have often been encouraging in cases which suffered repeated anginoid attacks.

Blood-pressure study of these cases needs to be correctly interpreted to give data of value. If the endarteritis has existed during a long period, has been extensive, has involved the renal and mesenteric vessels, there will probably be a high systolic pressure with a high pulse pressure, a tense and thickened radial pulse. These cases also have decided accentuation of the second aortic sound and often an aortic systolic murmur. The aorta is included in the process and shows the characteristic changes of *specific aortitis.* The result of blood pressure study alone in such a case is valueless, this must be added to all which the case presents before prognosis is justified.

Such cases as we have above mentioned are of serious character, they demand a guarded prognosis and before it is positively given, the effect of treatment should be studied. With some of these cases, the blood-pressure may be normal or reduced; such reduction is then evidence of myocardial weakness, and the prognosis is thereby unfavorably influenced.

Specific obliterating endarteritis may cause gangrene of an extremity or less striking trophic changes. We have found intermittent claudication, erythromelalgia, and symmetrical gangrene of the finger tips (Raynaud's disease), in which the underlying arteritis proved to be specific and in which rigorous treatment led to the recovery of some, and the material improvement of others.

Specific amyloid degeneration of small and large vessels is always serious; it is usually associated with similar degenerative processes in other vital organs, and is not often relieved by treatment. When the kidney is involved in a similar process and there is anemia gravis, but little hope can be given.

For the purposes of the prognostician, it is necessary to assume that all unexplained arteritides in young subjects should be suspected to be of syphilitic origin, and demand the refinements of diagnosis and therapeutic tests before final conclusions are reached. Naturally the prognosis of arteritis specifica depends largely upon the importance of the organs directly involved, and the influence of the changed relations.

Aortitis Syphilitica.—Specific aortitis may lead to aneurysm of the aorta; it may be associated with non-specific arteriosclerosis of the aorta, but its seat is characteristic in almost all cases during its early existence. Uncomplicated specific aortitis causes irregular thickening of the aortic wall (fibrous thickening), with patches of thinner tissue between these plaques. It invades the ascending aorta and the arch. There is a distinct line of demarkation which separates the changed aorta from the valve and tissues of the aorta directly above it. The prognosis is uncertain.

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Physical signs of aortitis and subjective symptoms often disappear under treatment.

There are according to Grassmann accidental or functional murmurs in 40 per cent of cases during the secondary stage of syphilis. In occasional cases during this stage, there may be threatening incompetence of the heart with low blood-pressure and dilatation of the right heart. Fever and anemia may be present. The prognosis is good in almost all of these cases. *One of the dangers occurs from suddenly arising pulmonary edema.*

Heart Syphilis.—There is no tissue of the heart in which specific disease may not cause organic change. We have mentioned coronary and aortic disease; the endocardium may degenerate, the aortic valves particularly may be the seat of specific deposit and change, the myocardium may be uniformly infiltrated and degenerated—it may hold one or more gummata—the pericardium may be involved; in all of these the Wassermann reaction is likely to be positive.

The Wassermann test has given us positive information concerning an enormous material which was formerly unexplainable. We refer to those heart lesions, the pathogenesis of which we did not understand—including especially the degenerative rather than the inflammatory processes—usually found during middle life when arteriosclerosis and disorganizing changes are unexpected. The larger number of these lesions are aortic, endocardial, myocardial and coronary. The aortic lesions are in the ascendency. *In over 50 per cent of these unexplained cases the Wassermann reaction is positive, and the prognosis is accordingly improved.* Aortic valvular lesions are found with positive Wassermann reactions in over 55 per cent of our cases.

There are unquestionably many specific lesions of the heart which never give rise to symptoms, which remain undetected, and are cured by the treatment of the constitutional infections, just as the large proportion of positive Wassermann tests of the cerebrospinal fluid and its cellular elements prove that changes in the nervous system may exist without subjective symptoms, which also disappear under similar conditions.

We have elsewhere called attention to the evanescence of physical signs, the disappearance of murmurs with positive organic disease. Recent additions to our knowledge, prove these cases to be of specific origin, and materially improve their prognosis (Elsner).

The prognosis of specific myocarditis depends on the length of its existence, the associated lesions, and the effect of specific treatment. Certainly the prognosis of the degenerative diseases of the myocardium due to syphilis is much better than non-specific disease. Harlow Brooks says: "Nearly all cases of syphilis are well treated at least for so long as mucous membrane or skin lesions present themselves; just as long as these show, the patient is willing to submit himself to treatment and to observation.

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Hence, it is that at least for a time, many or most cases of cardiac involvement are correctly treated even though unrecognized."

Lesions of the heart of specific origin, including degenerative myocarditis, valvular lesions, arteritis of the heart vessels, may become *latent;* they may "heal and resorb under proper medication." There are unquestionably many heart lesions during the early stages of syphilis which give rise to no symptoms—which unchecked would prove fatal—but which are stayed and cured by specific treatment. Cardiac lesions of late syphilis may often be threatening, the heart may be insufficient and yet under treatment there may be recovery or marked improvement. The prognosis cannot be given until the treatment has been sufficiently tested. Brooks says: "It is also true that a cheerful prognosis is not permissible until it has been determined just how much may be achieved by proper treatment. So frequently have I been deceived in both directions, that I now refuse prognosis until the case has been under treatment at least for a time—after which from the degree and character of the improvement or its failure, one may quite accurately prognose what may be expected with a further prosecution."

The *Stokes-Adams phenomenon* has in a few cases been found with *specific degeneration of the intraventricular septum* (His fibers); gumma have been found in several cases post mortem. Such cases offer a serious forecast, though improvement or recovery may follow rigorous treatment.

All cases of *infiltrating specific myocarditis* must be considered serious, and justify only a tentative prognosis until the horizon is cleared by treatment, including rest. Mracek gives the specific heart lesions which he found in 60 cases:

Gummatous myocarditis	10
Fibrous myocarditis	9
Gummatous and fibrous myocarditis	8
Endocarditis	2
Coronary arteries alone	3
Pericardium alone	1
Myocardium and pericardium	15
Pericardium, myocardium and endocardium	1
Myocardium and coronary arteries	1
All parts of the heart	6
Cardiac ganglia	4

(For further information concerning the fuller pathologic data which influence prognosis, the reader is referred to the works of Virchow and Mracek, above cited; also Hirschfelder, Huchard, Isaac Adler, Aschoff, Gruber and Stadler.)

Phlebitis syphilitica.—Changes in the veins may lead to phlebitis, phlegmasia alba dolens and erythematous nodes associated with fever and exacerbation of constitutional symptoms. In all of these conditions the prognosis is favorable.

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Syphilis of the Liver

Specific diseases of the liver are found with: (a) acquired syphilis, (b) congenital syphilis. Specific lesions of the liver are the most frequent of the visceral diseases found in the abdomen.

(a) **Acquired Syphilis of the Liver.**—Jaundice is not unusual during the secondary stage of acquired syphilis. The bile passages and liver parenchyma are invaded. The organ may be slightly enlarged. These cases run a benign course and recovery is the rule after a short period of treatment.

Acute Atrophy of the Liver.—Atrophy of the liver occasionally arises during the secondary stage of syphilis, and with all of the symptoms of rapid degeneration, jaundice, sepsis and heart weakness; these patients die within from forty-eight hours to three or four days. Rolleston has reported twenty-eight cases of postsyphilitic acute atrophy of the liver.

Gummata.—The liver invasion of the tertiary stage is usually *gummatous.* There may be interstitial infiltration and connective tissue proliferation with marked contraction resembling the atrophic form of cirrhosis of the liver. These are not so-called parasyphilitic lesions, but are due to the proliferation of the treponema *in situ.*

Specific diseases of the liver are usually associated with more or less *fever of an atypical type; and multiple gummata may lead to the suspicion of liver cancer and abscess.* With *nodules situated anteriorly,* the masses are palpable. There is wasting and progressive weakness with the fever. There is also pain and the enlarged liver is tender. With *disseminated nodules there* is usually ascites, more or less perihepatitis, and occasionally jaundice. *Perihepatitis* is an attendant of almost all liver gummata.

With *lues maligna* (malignant syphilis) amyloid degeneration of the liver with enlarged and waxy spleen and kidney invasion is frequent. Characteristic anemia accompanies these conditions.

The prognosis of uncomplicated gummata of the liver or specific hepatitis and perihepatitis is usually good. It is surprising to find how promptly these cases improve under modern treatment. Cases that have been neglected, with complications, particularly in those whose resistance is below par, are serious. Malignant lues above mentioned, with the associated liver complications, is always ominous; usually death is the result of widespread amyloid degeneration.

(b) **Congenital Syphilis of the Liver.**—Syphilis of the liver may be an early or a late complication of congenital syphilis (lues hereditaria tarda). The early manifestations are those of far-reaching hepatitis: the Treponema pallidum can be found in the liver tissue. There is at the same time invasion of the spleen and kidney: occasionally the pancreas shows marked fibroid change. These changes may be found in the still-

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born syphilitic child, or death may follow during the first week. Cases of congenital liver syphilis which develop early may occasionally, under prompt and rigorous treatment, recover; a grave prognosis should however always be given. With jaundice and ascites there is but little hope.

Lues Hereditaria Tarda.—The tardy form of liver lues is always an interesting condition which usually develops sometime between the tenth and twentieth year in subjects who have all of the earmarks of the constitutional infection well developed in the skin, teeth, bones, eyes, and in faulty growth. Arterial changes with marked narrowing of the vessels are usually present.

The physical signs referable to the liver are much the same as with the acquired forms of gummatous and interstitial hepatitis. Amyloid degeneration is usually widespread. The spleen is enlarged. Perihepatitis is almost constant. The majority of these cases are neglected; after long periods of indefinite symptoms. Death is the rule with symptoms of toxemia, uremia, etc.

Cirrhosis of the liver is not caused by syphilis, but there are cases in which syphilis of the liver may complicate and materially influence the course of the cirrhotic process. With congenital syphilis, changes which are differentiated from cirrhosis with great difficulty, are found. They offer a grave prognosis.

The prognosis of all forms of liver enlargement or of liver lesions will, in a surprising number of cases where serious non-specific disease is suspected or even diagnosticated, be favorably influenced by specific treatment. This is a dictum of great importance.

Syphilis of the Kidney

During the secondary stage of the disease as already mentioned, nephritis may develop. It usually appears with the roseola eruption. The features are those of acute tubal nephritis (parenchymatous), with dropsies and abundant albuminuria and casts. These cases are usually amenable to treatment, and recover. Neglected cases die of uremia with myocardial invasion as a rule. Occasionally subacute and chronic nephritis originates during the secondary stage.

Tertiary syphilis may lead to *gummatous deposit* in the kidney, when there may be physical and subjective manifestations of renal tumor. Chronic interstitial nephritis may be associated with specific arteritis and specific heart changes (myocarditis). There are mixed forms of nephritis, also amyloid degeneration, with similar changes in other organs of the body. Interstitial nephritis and waxy or amyloid kidney are the most frequent kidney changes of tertiary syphilis and are never to be lightly regarded; they offer a serious prognosis. The *gumma of the kidney improves* and its size reduces with return to normal, after a sufficient period

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of rigorous treatment. Scars are found in such kidneys—proving the possibility of cure.

Syphilis of the Testicle and Epididymis

Early swelling of the testicle and epididymis of specific origin are promptly influenced by treatment, and lead to full recovery without injury to the organs infiltrated. The late manifestations of syphilis usually limit themselves to the testicle; the epididymis escapes. The late processes may be either gummatous or there may be a diffuse interstitial infiltration of the organ, or both forms may be together (Scholtz).

Scholtz calls attention to the fact that even with relatively early treatment the functions of the testicle may suffer; spermatozoa may disappear (azoöspermia) or they are much reduced in number (oligospermia). If the disease is neglected, aspermia may result (Scholtz). In most cases the prognosis is good, and complete restoration of function results with a remnant of scar tissue in the testicle.

The syphilitic diseases of the genitalia in both sexes—the bladder and the urethra are exceedingly rare—are surgical affections, and their consideration is therefore omitted. In passing, it may be said that they offer favorable prognosis.

Syphilis of the Bones and Joints

Syphilis of the bones and joints belongs to the domain of surgery.

Syphilis of the Muscles (Myositis)

The various forms of specific myositis all yield to treatment. When neglected, atrophy may result.

Syphilis of the Respiratory Organs

Nasal Syphilis.—We have already, in connection with the consideration of gummatous deposits, considered nasal syphilis. The remaining nasal lesions are surgical, and offer favorable prognoses only when treated early. The destruction of tissues goes on unobserved, insidiously, until there is irreparable injury and deformity. *Labial and pharyngeal gummata* may cause tissue loss, and the *deep ulcerations of the pharynx* may lead to adhesions and consecutive symptoms. In smokers these lesions may heal slowly, and leukoplakia with mucous patches may be constantly present in such mouths during many years.

There are occasional cases of malignant syphilis in which these lesions refuse to yield to any form of treatment: glandular enlargement increases, there is a hard infiltration of the glands (sublingual and submaxillary)

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with invasion of the surrounding tissue, ultimate breakdown of tissue, increasing anemia, and final cachexia—the patients dying with all of the symptoms of malignant disease absolutely uninfluenced by any treatment, as already mentioned. These cases are among the most rebellious which we have encountered in connection with syphilitic disease.

Laryngeal Syphilis.—The appearance of syphilitic laryngeal lesions is at once associated with subjective symptoms, which in consequence, usually receive early and successful treatment. The larger number of lesions are of secondary origin. Gerber reports that laryngeal syphilis represents 4.5 per cent of syphilitic lesions and 3.6 per cent of all diseases of the larynx.

The *gummata of the larynx* when neglected, as they are found in the tertiary stage, may lead to deep and irreparable ulceration, cicatrization and malformation, due to adhesions.

Stenosis of the glottis and cartilaginous destruction may complicate and add to the dangers. Suddenly arising *edema of the glottis* in occasional cases, may prove life-threatening, and unless promptly relieved ends fatally. *This may follow the injection of salvarsan and prove to be a true Herxheimer reaction; a fact of enormous importance.* Relapses of laryngeal syphilis are frequent, though the ulcerative process usually yields to treatment promptly.

Syphilis of the Bronchi and Trachea.—*Bronchial and tracheal syphilis* is rare. Occasionally there are secondary ulcerative lesions which yield promptly. Tertiary lesions of the bronchi and trachea may, if undetected, lead to ulceration and stricture with serious results.

Syphilis of the Lung.—Syphilis of the lung is rare, and is an evidence of tertiary disease. It may be either gummatous—usually multiple—or it may be interstitial, and lead to chronic pneumonia. (See Interstitial Pneumonia; also the chapter on Tuberculosis showing the influence of syphilitic infection on the prognosis of pulmonary tuberculosis, where this subject is fully considered). *Gummata of the lung* are favorably influenced by treatment and offer a fairly good prognosis. Widespread *interstitial changes in the lung* are but little influenced by treatment. Such cases offer the same prognosis as do the other chronic types of pneumonia (See Chronic Interstitial Pneumonia).

Syphilis of the Spleen

The spleen may be enlarged during the secondary stage; there is usually fever and an exanthematous eruption. Hoffman claims to be able to demonstrate the Treponema in the spleen by puncture at this time (Scholtz). This enlargment is not significant prognostically.

Gummata of the spleen accompany similar liver deposits, and offer the same prognosis as does liver syphilis. The spleen may be enlarged, or

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the gumma may be so located as to cause no great change in the form or size of the organ. With lues maligna, the spleen may undergo *amyloid degeneration.* This is a part of a general process in which liver, kidney and blood-vessels are involved. The prognosis is unfavorable.

Most forms of syphilitic disease of the spleen are evanescent and offer good prognoses.

With congenital lues there may be *chronic enlargement of the spleen with characteristic anemia.* This may develop early. The spleen may increase to ten times its normal weight (Aschoff). These cases are amenable to treatment: many make permanent recoveries. When enlarged spleen is coincident with hepatitis in the subject of congenital syphilis (syphilis hereditaria tarda), the prognosis is not good.

Syphilis of the Digestive Tract

Syphilis of the Rectum.—The rectum is more frequently the seat of specific lesions than any other part of the digestive tract, and these may be present during any stage. *Primary lesions* are occasionally found in the rectum which lead to ulceration, and make differentiation difficult; such lesions heal without leaving remnants. *Secondary rectal lesions* offer a good prognosis; the mucosa is not permanently damaged and heals promptly under treatment. *Tertiary lesions* may cause deep changes and stricture if neglected.

There may be simple gummatous deposits with ulcerations, or a productive proctitis with considerable thickening and persistent subjective symptoms. The connective tissue proliferation with accompanying thickening and ulceration in the infiltrating form of specific proctitis is often rebellious to treatment; in some, the rectum is finally converted into a thickened, uneven, and narrowed tube with stricture formation, periproctitis, consecutive anemia and resulting chronic invalidism.

Syphilis of the Stomach.—The dyspeptic symptoms of the secondary stage are evanescent. Tertiary lesions when present, rarely cause symptoms which lead to their detection. Fournier has reported such cases, and recently Jerome Meyer has made an exhaustive review of this subject. We know of no serious results which have followed the stomach lesions of syphilis in our practice. Possibly an occasional gastric ulcer may be of syphilitic origin.

Syphilis of the Esophagus.—Esophageal ulcers are rare and usually heal; in exceptional cases stricture of the esophagus has been found in syphilitics, without the history of previous ulceration.

Syphilis of the Intestines.—Intestinal lesions of specific origin are also exceedingly rare. When suspected, without positive history, the Wassermann reaction and a therapeutic test may be needed. We have had no experience with intestinal syphilis.

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Syphilis of the Nervous System

There are inviting factors which lead to syphilis of the nervous system; among these are alcoholic excess, overwork, and the worry which is associated with the stress of modern life (Edinger). The influence of these factors is denied by some, but the weight of experience strengthens the contention that they do exert a powerful influence.

The prime factor, as will be accented in considering cerebral syphilis, is insufficient or faulty treatment during the early stages of the infection. The mild early infections, because of their rapid relief and short treatment, are oftener followed by nerve syphilis than are those with the more serious initial lesions. The lesions of the nervous system (excluding paresis and locomotor ataxia) may appear early or late: the average time is between one and four years after the primary infection. With our present method of treatment it would appear that the early cases, radically treated, will prove to be the more tractable.

At least 15 to 20 per cent of all syphilitics—until the introduction of salvarsan and the modern treatment of syphilis—developed specific disease of the nervous system. *It will require at least two decades of observation to reach conclusions which justify figures based on the newer therapy of Ehrlich, and mercury.* The most encouraging statement which we can make at the present time is that the outlook seems encouraging. If the recently made observations of Noguchi which seem to prove the presence of the Treponema pallidum in the brain of paretics are corroborated, paresis and tabes must be included among the tertiary lesions of syphilis.

Syphilis of the Spinal Cord.—The manifestations of syphilis of the cord are numerous, and it is exceedingly difficult to offer a single clinical picture which includes all of its possible manifestations. In considering the prognosis of the lesions of the nervous system, especially of the cord, it must be remembered that *there is no proof that syphilis ever causes any of the functional diseases of the nervous system.*

Spinal syphilis tends to indiscriminate lesions with the inclusion of meningeal and cerebral changes. Spinal syphilis as shown by lumbar puncture is a frequent complication of tertiary syphilis; its diagnosis can be positively established by the Wassermann reaction of the blood and the examination of the cerebrospinal fluid.

There are occasional cases of spinal syphilis which cause positive symptoms within one month of the initial infection; as a rule from three to five years lapse before the spinal lesions of syphilis develop subjective symptoms.

Spinal syphilis during its course is *characterized by remissions and exacerbations;* for this reason threatening symptoms do not have the same prognostic significance as they do with non-syphilitic disease of the cord in which the prognosis is less favorable. With spinal syphilis, the multi-

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plicity and incompleteness of symptoms are characteristic. Oppenheim accents "the instability, the coming and going of symptoms." Paresis of one or both legs may develop suddenly, and promptly increase to paraplegia, or paresis of one limb may remain. Spinal syphilis is a protean disease: its typical form includes *sensory* and *motor symptoms*—usually specific, partial paraplegia—with bladder invasion in some cases. Oppenheim describes a "pseudotabes syphilitica," in which the disease extends to the posterior roots and column.

So far as life is concerned, the prognosis of the majority of these cases is good; complete *restitutio ad integrum* is not often reached, for there are secondary changes which result from compression and scar tissue, and in cases which mend, are likely to leave permanent weakness of the lower extremities. As a rule bladder function is restored in the favorable cases.

There is always danger in these cases of sudden and severe exacerbation of symptoms, associated meningo-myelitis; the brain symptoms may suddenly gain the ascendency, and death follows within a few days or weeks. The prognosis is always graver in those cases in which brain symptoms are present either from the beginning, or develop gradually or suddenly. Such cases may develop and lead to death during periods of latency.

I feel that, with the positive results of cytological examinations;—the four reactions, i. e., (1) Nonne reaction (globulin + Phase I (2) Wassermann reaction (within the blood) (3) Pleocytosis (lymphocytosis) (4) Wassermann reaction (in the spinal fluid)—cases will come under earlier treatment, and the prognosis will be accordingly improved; that there will in consequence be fewer advanced cases and less permanent damage.

Cases in which there are far-reaching changes in the arteries (endarteritis obliterans) and veins, lead to myelitic softening and permanent loss of function.

Spinal syphilis may run its course with all of the symptoms of an acute dorsal or dorsocervical meningitis. In these cases the prognosis depends on the extent of the specific changes, the stage of the disease, the reaction to treatment and the strength of the patient. We have seen a number of cases in which recovery followed; some of our cases developed cerebral symptoms and died. In one, the spinal symptoms yielded, the patient fell into a somnolent condition, in which she remained during a number of weeks, and under rigorous specific treatment (mercurial inunction), recovered completely.

Spinal lesions which limit themselves to the nerve roots and meninges, without involving the substance of the cord, offer a good prognosis in a large proportion of cases. These are the more favorable cases of spinal lues. *Whenever the cord substance has degenerated the prognosis for res-*

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toration of *function is bad.* *Paraplegia* of short duration, promptly subjected to treatment, offers a fair prognosis.

The prognosis of specific spinal paralysis is materially influenced by its extent and the time of its existence. *Spastic contractures* with such paralysis, and exaggerated reflexes argue against relief by treatment.

A large number of the cases of spinal syphilis included in our consideration, correspond exactly with the complex now known as *"Erb's syphilitic spinal paralysis"* to which Erb called attention in 1892. The paralyses are always spastic; the tendon reflexes are exaggerated; the tension of the muscles themselves is not markedly increased. There are paresthesias and girdle sensation without pain, save in occasional cases. The bladder and rectum are involved in advanced cases. Erb's syphilitic paralysis is chronic; it tends to improve; there are long periods of remission and in many cases the process remains stationary—covering a period of many years.

Relapse, years after improvement or cure, is not infrequent.

There are cases of spinal syphilis which remain uninfluenced by any treatment, progress either insidiously or as may happen, run an acute course, ending in a few weeks.

Acute tertiary lesions of the spine added to so-called metasyphilitic disease of the nervous system offer an unfavorable prognosis.

Hereditary types of cerebrospinal syphilis may lead to indiscriminate and chronic lesions which are but little influenced by treatment; occasionally Oppenheim claims to have seen satisfactory recoveries.

Syphilitic Peripheral Neuritis.—There are occasional forms of syphilitic peripheral neuritis; the ulnar nerve is invaded by predilection.

Syphilitic poison does not show marked affinity for the nerve trunks but we have met a number of cases which prove the possibility of such invasion, in all of which, the prognosis was good.

Evidences of compression of separate nerves of the periphery, due either to the pressure of specific exostoses or to gummata, may yield to treatment.

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Cerebral Syphilis.—The frequency and great importance of syphilitic infection as a cause of grave disease of the nervous system is promptly appreciated when we consider the results of lumbar puncture, which offer positive evidences in characteristic change in the fluid, of the existence of such complication. The results in over 1,400 lumbar punctures made and reported by Dreyfus at the Städtisches Krankenhaus in Frankfurt a/M. are instructive. It was found that during the early period of syphilitic infection the lumbar fluid showed positive involvement of the nervous system (brain and spine) in 80 per cent of all such cases, and that 12 per cent of all latent syphilis showed positive syphilitic disease of the central nervous system in characteristic changes in the lumbar fluid withdrawn. By this method therefore—the appreciation of the significance of its revelations and the rigorous modern treatment of the disease—the prognosis of cerebral and all metaluetic infection is being favorably influenced. In a lecture which Ehrlich delivered (January 16, 1914) on the difficulties which he was forced to overcome in bringing his remedy to its present usefulness and safety, he made the positive statement that, guided by the results of lumbar puncture, the

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clinician was now in position to positively prevent the development of paresis and tabes by the intensive treatment of the infection.

General Consideration of Cerebral Syphilis.—The separate types of cerebral syphilis offer a varying prognosis, yet it may be wise in a work of this character to follow the example of Nonne as set forth in his lectures on syphilis of the brain, to devote a short chapter to the general consideration of the subject.

It may be assumed that all types of syphilitic disease, as it invades the brain, are of serious import and frequently lead to death; often, to a chronic state of complete or partial incapacity persisting during years; while in a number of cases the disease may be followed by complete restoration to health—physical and mental. It may be assumed further that syphilis of the brain offers a more favorable prognosis than most non-syphilitic diseases of that organ, including more particularly brain tumor, abscess, multiple sclerosis and degenerative changes associated with paralysis; this is true when the diagnosis is made early.

Comparing the results of the operative treatment of brain tumors, we find, in the event of the prolongation of the life of the patient, that recovery is not likely to be complete; that as a rule the symptoms have not been materially relieved. Single abscess of the brain is rare; usually there are multiple lesions; as Nonne emphasizes in his comparison of the prognosis of these conditions, there is likely to be secondary meningitis. Multiple sclerosis and secondary paralyses lead to death sooner or later, either directly or frequently indirectly, from distant invasion—heart, lung, sepsis, etc. These facts justify the statement above made that specific brain lesions when recognized early offer a much better prognosis than do those of non-specific nature.

Paresis is not included in our consideration of brain syphilis, this will receive separate treatment. We wish to include in this chapter, brain syphilis in which the symptoms are dependent upon specific meningitic invasion, gummatous infiltration and specific arteritis. Fournier reports that $\frac{1}{3}$ of his cases are cured, $\frac{1}{2}$ are materially improved, and $\frac{1}{6}$ die. In Rumpf's analysis of 34 cases he found 31 justifying conclusions; of these latter, 5 died, 8 remained incapacitated and sick, improvement followed in 6 cases, and 12 made full recoveries. Hjelmman on the other hand holds that his experience justifies the conclusion that one-half of his cases proved fatal or fell into hopeless conditions, that the fully cured cases were not above 25 per cent, while in the remaining cases there was only partial improvement.

My experience justifies the conclusions that have been advanced by Fournier and Rumpf. The time of recognition of the disease becomes an important factor; in no other disease of the nervous system is this more vital. Further, it must be agreed that our free recourse to modern methods of diagnosis, including *blood tests* (*Wassermann*) have influ-

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enced the prognosis of cerebral syphilis very favorably, and our statistics are therefore more encouraging than ever before.

The examination of the spinal fluid shows that there is lymphocytosis, the globulin reaction, some leukocytosis and the positive Wassermann reaction. The albumin content is slightly increased. Pressure increased.

Phase I, or the globulin reaction with the saturated ammonium sulphate solution, is only present when there are symptoms of central nervous disease. Decided change in the lumbar fluid after treatment and a return to a negative Wassermann may be interpreted as being favorable.

From both hospital and private practice we are able to furnish many examples of cerebral syphilis in which there has been no return of symptoms during many years—varying from two to twenty, and even longer. It must be further conceded that with increased diagnostic ability we have traced a large number of cerebral symptoms to syphilitic infection, have treated these rigorously, and have in consequence materially changed our statistics.

Adopting, as does the modern clinician the two underlying pathologic conditions as the leading causes of symptoms in cerebral syphilis—the first so thoroughly described by Virchow in 1858, which includes those lesions of *gummatous nature* with meningeal invasion, and the second, which proves the presence of specific *arteritis* included in the classic description of Heubner in 1874—it becomes possible to plant our diagnosis, prognosis and treatment, upon a safe foundation.

The analysis made by Naunyn of his own 88 cases and 325 collected from medical literature (total of 413 cases), proves profitable and interesting. Naunyn considers cases "cured" which show no recurrence after five years of apparent health. He found seven such cases in Caspary's material, 3 in Fournier's; his own included 10 cases; while Oppenheim in his monograph reports seven cases of complete cure 5 and 10 years after the last attacks. Nonne presents a material of 124 cases of cerebral syphilis in which symptoms were limited absolutely to the brain. Of this number he was able to follow only 22 cases 5 years, 4 cases over 5 years. Of this latter number two cases followed six years, one seven, one eight years—all remaining without recurrence of symptoms.

It may be accepted as true that in the majority of cases supposedly cured, unless treatment continues to be rigorous and the patients are properly led and safely guarded, they fall into the larger class of the partially cured.

My experience justifies the conclusion, that cerebral syphilis which has remained uncontrolled or untreated during a period sufficient to lead to paralysis with associated degeneration of brain tissue, whatever the type, is never fully cured; and though treatment may improve existing symptoms in a measure, the damage is permanent and the patient often develops sudden exacerbation which may lead to death.

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Many cases live for years with symptoms of secondary degeneration. Some are tied to a mattress grave. Neurologists are agreed in considering the prognosis of cerebral syphilis, that in no cases apparently cured can we be certain of freedom from relapse. "Syphilis never dies, it only sleeps" (Nonne). *Relapses* may include acute *endarteritic attacks, specific meningitis, fresh gummatous deposits;* and these may alternate with each other in a single case.

I have seen long periods lapse between attacks; in malignant cases one type may follow the other with but short intermission, patients finally yielding in coma to specific meningitis.

The study of our own material justifies a more serious prognosis in the cerebral syphilis of advanced, than during early life. *Age* has seemed to be without marked influence until about the 45th to 50th year, after which, because of greater tendency to *arterial degeneration,* resistance to treatment has increased and its effect has become less efficient and slower. (Ricord, Fournier and Mingazzini report similar experiences.) Malignant types of brain syphilis are not infrequent among young subjects; many of these are found with the added depressing effect of dissipation in venery and alcohol.

Interval Following Specific Infection and the Development of Cerebral Syphilis.—Long postponed cerebral syphilis offers a less favorable prognosis than does the development of brain lesions before the end of ten years (Hjelmman, Naunyn, Nonne). *Heredity* does not seem to influence the prognosis of cerebral syphilis. Neuropathic tendencies have not invited or influenced the development of the brain complication.

Tuberculous and anemic individuals, the *cachectic* and generally reduced—particularly those who, weakened by *alcoholic excess,* are not good subjects—offer scant resistance to the advance of cerebral lues. It has seemed to us that the most malignant types of cerebral syphilis met in our practice have followed *alcoholic meningitis* or *wet brain,* which in turn complicated *delirium tremens.* Most of these were seen in hospital wards; were neglected and among the lower classes. Tarnowsky found in 100 cases of pronounced cerebral syphilis, 43 chronic alcoholics, many neurasthenics, some cases of skull injuries, and a good number of patients overtaxed mentally; and he believes that these factors are of paramount importance in the prognosis of the disease. This would also corroborate the theory of Edinger. My experience does not include a single case in which I have reason to believe that trauma was a provocative factor, or directly influenced prognosis.

The author is in accord with Byron Bramwell who has demonstrated the fact that the graver forms of nerve and brain syphilis follow the milder types of the initial disease. This is simply due to the early disappearance of visible lesions and the resulting neglect of treatment of these milder cases. Fournier believes that there is a form of syphilis which by

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predilection attacks the nervous system: *"syphilis a virus nerveux."* That there are such cases, there can be no doubt. They may appear early or late; they are likely to remain unaffected by treatment. They may follow the so-called milder infections or cases which show malignant tendencies *ab initio*. The location of the initial lesion has not seemed to influence the prognosis of any specific complications in our experience.

Rational and early modern treatment has during the last five years materially influenced the prognosis of cerebral syphilis and all nerve complications of syphilis, and unless I misinterpret my experiences, has already reduced the number of these cases. In this connection the statement of Hjelmman is of vital importance, if correct: "In from 82-88 per cent, patients with symptoms of cerebral syphilis have had either no treatment or insufficient treatment," and he believes as we all have reason to do, that in the majority of these cases rational treatment would have prevented the serious condition.

There will always be a remnant of cases in which, in spite of early and persistent treatment, syphilitic lesions whether cerebral or not, will remain rebellious and refuse absolutely to yield. In the majority of these, careful search will reveal the cause, but the therapeutist will be unable to antagonize it successfully. Nonne, however, believes that cases of brain syphilis offer no better prognosis, in spite of the fact that they were scientifically treated—mercury, etc., administered during several years—than do those cases in which the early treatment was neglected or entirely omitted. Cases of *specific localized meningitis* associated with long periods of somnolence, frequently remaining unrecognized—splendidly pictured by Buzzard—offer a very favorable prognosis. To the inexperienced, the clinical picture may appear exceedingly alarming. Naunyn, Hjelmman and Oppenheim place basilar meningitis of specific origin in a class offering a good prognosis (71 per cent). These cases, it has been our experience, may relapse, but in the end they seem to make good recoveries.

Diffuse deposits do not as a rule offer an encouraging outlook. The changes are not limited to the brain; there are likely to be indiscriminate lesions in distant nerve tissue. The early diagnosis is not easily made; the cases are therefore misunderstood during considerable periods.

Syphilitic epilepsy with focal symptoms is in the majority of cases favorably influenced by treatment, and recoveries are not infrequent.

Early recognized *single gumma* will in most cases show marked improvement under treatment, and while a complete anatomic cure may not be certain, clinically the large majority of these cases has yielded and has remained without serious complications, though in none does the prognosis justify cessation of eternal vigilance.

I have already referred to the Huebner type of *specific endarteritis*. Gummata of the arteries are not of frequent occurrence. In the Huebner

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type of arteritis, the inflammatory infiltration of the vessel wall may be absorbed, the narrowing of the lumen may not be materially reduced, but the extent of brain tissue involved is likely to be limited; and though it may not regain its power, there will as a rule be compensation sufficient in most cases to supply function. I have seen cases diagnosticated as *arteritis specifica,* with hemiplegia, which have yielded after several weeks of persistent symptoms. In the majority of these cases the patients recover with clear intellect and memories, are undisturbed, though there may in the severe cases, be some motor weakness with few sensory symptoms left. *Hemiplegia,* however, with syphilis should never be lightly considered; it is always serious.

In cases associated with renal changes, *chronic nephritis* and *hypertension, the prognosis* must of necessity be grave.

Recurrences are not infrequent, if there are many or if there is continuous progression of arteritis, the patient falls into a pitiful condition—paretic and hopeless.

Cases of specific arteritis (Huebner) do not as a rule die suddenly or early. When the process invades the basilar vessels, the prognosis is most grave because of the invasion also of the higher psychic centers.

It is occasionally difficult to differentiate *paralysis of the motor oculi* of arteritic and gummatous origin. The former offers a less favorable prognosis so far as complete restoration of function is concerned. Ordinary syphilitic paralysis of the motor oculi, usually gummatous, is likely to disappear completely under treatment. Optic neuritis (choked disk) does not argue against the possibility of recovery; advanced optic atrophy with cerebral syphilis is always evidence of serious disturbance, and the prognosis is consequently bad.

Long continued paralysis of the cranial nerves, with syphilis of the brain, offers an unfavorable prognosis for restoration of health or function.

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Late Manifestations of Tertiary Syphilis of the Cord and Brain—So-called Metasyphilitic Disease

The manifestations of the tertiary stage of syphilis which I include in my consideration, have until the present time been considered to be metasyphilitic—not dependent upon syphilis primarily—but the conditions were supposed to develop in syphilitic subjects in whom it was assumed that the brain and cord were possibly vulnerable, or that for some unknown cause degenerative and atrophic changes were invited.

With increasing clinical experience and pathological study, a strong suspicion had arisen in the mind of experienced neurologists and syphilographers that the relation of metasyphilitic diseases to specify syphilitic infection was one of direct cause and effect, and during several decades the French school led by Fournier, and the German school of which Erb was the Nestor among the neurologists, fought an active battle to establish the direct pathogenic relation of syphilis to tabes, paresis, and taboparesis.

Statistics gathered from the authoritive medical centers of both continents strengthened the contentions of Erb and Fournier, that in over 90 per cent of all so-called metasyphilitic disease, a clear history of syphilis could be established and that syphilis therefore was the prime factor to be considered in the prognosis and treatment of these diseases. Even the strong opposition of such authorities as Charcot, Westphal, von Leyden, and J. A. Glasser, did not influence Erb nor Fournier, who, persistently, by their writings and in their clinics, added material to strengthen their views.

The profession had registered itself in favor of the syphilitic pathogenesis of the metasyphilitic diseases and was fully prepared to receive the results of the epoch-producing experiments of Noguchi, which demonstrated the Treponema pallidum in the cord of tabetics and in the brain of paretics.

With these positive proofs of the presence of the Treponema, and the results of inoculation experiments by which similar conditions have been produced, and the further overwhelming evidence offered by the positive Wassermann reaction of the blood and by the spinal fluid (withdrawn by lumbar puncture), I feel justified in placing the conditions formerly included among the metasyphilitic diseases in the section on Syphilis. I believe that such classification will do much to justify the intensive

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treatment of syphilis, and will consequently favorably influence the incidence of tabes and paresis; further, I am fully satisfied that the infected, when aware of the true cause of the most dreaded of all of the complications of syphilis, will be more eager than ever before for such radical treatment as is demanded in the individual case.

We consider: (1) tabes dorsalis (locomotor ataxia), (2) taboparesis, (3) paresis (progressive paralysis of the insane).

Tabes dorsalis
(*Locomotor ataxia*)

The prognosis of locomotor ataxia has been powerfully influenced by the introduction of the newer methods of treating syphilis, the discovery of the Treponema in the cord and brain of tabetics and paretics, and the revelations of sero- and cytodiagnosis. Several years must lapse before positive conclusions can be justified.

The characteristic and constant lesion of locomotor ataxia is the grey degeneration, probably developed after a limited period of irritation—possibly inflammation, of the posterior columns of the cord. The disease is primarily a system disease of the cord, but its many manifestations soon prove its indiscriminate tendencies.

There are occasional *juvenile forms* of the disease due to congenital syphilis. As a rule tabes is found in the male, three times as often as in the female, and between the thirtieth and fiftieth years, and from 5 to 20 years after infection, with an average of 9 years.

Tabes within one to five years after initial infection has in my experience developed rapidly, and has usually entered the ataxic stage early. These cases offer a less favorable prognosis than do those which follow infection after a longer time.

In a fully developed case the following conditions may prevail:

1. The membranes of the cord are thickened over the part involved—more posteriorly.
2. There is flattening of the cord.
3. With degeneration, the posterior columns and nerves are shrunken and atrophied.
4. Connective tissue proliferation in the postero-external columns and posterior horns.
5. The disease attacks the dorsal and lumbar regions by preference.
6. With the onward march of the disease, the postero-internal columns and the posterior horns may be involved.
7. There are likely to be degenerative changes in one or more of the cranial nerves—the optic and motor oculi are oftenest involved. These changes may be either early or late.

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8. During the terminal stage the anterior horns and the lateral columns may be invaded, leading to atrophy of muscles and contractures.

9. There may be chronic arteritis invading the vessels of the cord and brain.

10. The terminal stage may include paresis or other cerebral lesions —hemorrhage, thrombosis, pachy—and leptomeningitis, and changes in the ependyma.

11. Aortitis, arteriosclerosis or arteritis are frequent complications, depending upon the same initial cause. The rapid development of arterial degeneration in tabetics of all ages is often surprising. The artery is uniformly thickened—shows placque deposits, and aortitis in such cases is usual.

The prognosis of locomotor ataxia must include the consideration of its (a) cause; (b) sex; (c) age; (d) possible prophylaxis; (e) location and extent of the degeneration; (f) the influence of the treatment on the symptoms of the various stages of the disease—initial, ataxic and paralytic; (g) the prognostic significance of individual symptoms; (h) Wassermann reaction of the blood and spinal fluid; (i) the complications.

(a) Causes.—In the light of our present knowledge, it is safe to assume that locomotor ataxia is always due to luetic infection. Basing the consideration of the disease upon this assumption strengthens the hope that with the dissemination of knowledge and the radical early treatment of those infected, the late manifestations referable to the nervous system will decrease in the future.

Fournier reported that in one thousand cases of locomotor ataxia, he found 92.5 per cent syphilitic. Erb found in 1,100 cases of locomotor ataxia among men in good condition, 89.4 per cent syphilitic; and in 158 workmen, 77.2 per cent syphilitic; 6,000 cases of nervous diseases, other than tabes, show 20 per cent of syphilitics.

Congenital and unrecognized syphilis was considered the cause of tabes in the small and unexplained remnant by both authorities; and with our present methods of diagnosis this conclusion is justified.

In Germany, Virchow in his Krankhaften Geschwülsten—a work far in advance of its time—insisted, before either Fournier or Erb had offered their conclusions, that "there is no doubt of the fact that some cases of tabes are syphilitic." For more complete statistics showing the relation of syphilis and tabes the reader is referred to Nonne's classic work; also Rumpf. The statistics of all large clinics gathered during the past decade fully corroborate the early conclusions of the French and German School.

The so-called metaluetic diseases including locomotor ataxia—either by their history, when thoroughly considered, or as the result of cytoserodiagnostic methods—establish syphilis as the cause in most cases (92 to 97 per cent).

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PREDISPOSING FACTORS.—There are factors which predispose syphilitics—acquired or congenital—to tabes; among these are improper treatment of the initial infection, hereditary tendencies and diathesis, exposure, excesses in alcohol and venery, traumatism, overwork, and worry. The theory of Edinger that the various parts of the nervous system yield to disease in proportion to the fatigue (exhaustion) resulting from overwork and the many other factors of life which, through the emotions and long continued wear and tear of an organ, prepare for surrender and ultimate pathologic degeneration—is plausible and deserves consideration.

(b) Sex.—The influence of sex on prognosis is insignificant. Collins believes that the disease advances with greater rapidity in women; this is not the accepted view. I have found that women fall into the same chronic stages as men and are subject to the same complications. Our cases show a larger number of paralysis of the eye muscles in women.

(c) The Influence of Age.—Pathologically juvenile tabes does not differ from the disease as found in the adult; both the symptoms and complications are identical though their development is different.

Syphilis is the cause of juvenile tabes; girls are oftener affected than boys. In juvenile tabes, optic atrophy with consecutive blindness is an early symptom, while lancinating pains are not as frequent as in the adult; the same is true of paresthesias and analgesias. Fully developed ataxia is exceptional; the course of the disease is protracted, but mild (Koester). Blind children are often found in public institutions with *juvenile paresis:* not an infrequent sequel.

There are occasional acute cases which run a rapid course in patients between the ages of twenty and thirty. The younger the adult, the more likely is the process to show rapid progression. One-half of all cases between 20 and 40 progress rapidly. After the fiftieth year, acute cases are unusual and chronicity is the rule. Tabetics often reach old age, as is shown by the statistics offered in considering the duration of the disease.

(d) Possible Prophylaxis.—For the future of the syphilitic, the possibility of the prevention of the late manifestations of disease of the brain and cord is of the utmost importance. The clinical experiences of the past prove that it is the rare exception for thoroughly treated cases of syphilis during the early and late stages to develop either tabes or paresis.

It is the untreated, usually mild cases in which the initial lesions were either hidden, unrecognized, or evanescent, and which received practically no treatment during the secondary stage of the disease, which later develop the most serious complications; and when the nervous system is included, the progression of symptoms is as a rule so insidious as to remain unrecognized until grave and irreparable degeneration proves the presence of advanced disease. The further evidence offered by repeated examination of the lumbar fluid during the early stage of syphilis, proves that the

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intensive treatment at once overcomes the incipient invasion of the brain and cord.

Dreyfus has demonstrated, after over 1,400 lumbar punctures, that the nervous system, i. e., the brain and cord, gives positive evidences of change in 80 per cent of all cases of early syphilis, and that in 12 per cent of syphilitics the reactions are positive during the late stages. It is the 12 per cent of uninfluenced cases which cloud the prognosis, and these are among the subjects who develop tabes and paresis when one or more of the exciting factors already mentioned prevail.

The small proportion of syphilitics who develop tabes and paresis also argues in favor of the prophylactic influence of the radical and intensive treatment of the initial disease. In private practice, where there is an intelligent coöperation of the patient and the physician, I have less than one per cent of so-called metasyphilitic infections to report. The average reported by Scholtz is from 2 to 3 per cent; this includes the material of hospitals, etc. Reumont found 40 cases of tabes in 3,600 syphilitics—1.1 per cent.

It is, according to well-digested experience, fair to give almost positive assurance of escape from the late manifestations of the tertiary stage of the disease, provided that the treatment of the preceding stages has been intensive and appropriate.

The profession is passing through a period in which positive conclusion with regard to the future of the syphilitic treated with salvarsan and mercury combined, cannot be given; the time for a safe forecast has been insufficient. To be certain that the late manifestations including tabes will be entirely prevented will require a period of observation, covering at least three decades. The indications, however, are favorable and those who have had the largest experience justify an encouraging outlook. Ehrlich believes "that the early intensive treatment of syphilis with salvarsan and mercury will practically prevent the occurrence of tabes, taboparesis and paresis."

(e) The Location and Extent of the Degeneration.—The prognosis is worse in cases which are associated with multiple or disseminated cerebral lesions; worse also so far as comfort and progression are concerned, the higher in the spine the degeneration spends its force; bad with cervical and bulbar invasion.

The prognosis is absolutely bad when paresis complicates tabes; also with other psychoses.

Reference to lesions of the peripheral nervous system, the brain and sympathetic system are found in the separate chapters dealing with these.

(f) The Influence of the Treatment on the Symptoms of the Various Stages of the Disease.—We consider an (1) initial stage (neuralgic—preataxic, (2) ataxic stage, (3) paralytic stage.

1. The Initial or Neuralgic Stage.—Locomotor ataxia may re-

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main stationary in any stage of the disease—oftener in the first stage—with or without treatment. The increasing benign tendencies of certain types of the disease was recognized by Charcot and Brissaud because of the growing frequency of mild cases which show but little tendency to progress, and remain latent or stationary during several decades, in some instances. This fact has led to the conclusion that tabes is less serious to-day than in the past: a fact which unquestionably depends upon the more thorough and scientific treatment of the early stages of the disease. Oppenheim believes that there is in tabes, as in many other diseases, a lowering of the malignancy of the infection with succeding generations. The older neurologists including Duchenne, Romberg, Trousseau and Charcot during his early experiences, as well as Leyden as late as 1878, considered the disease to be always progressive, and rarely recognized the cases which have increased in frequency, with a duration often of 15 to 30 years or even longer. It may be assumed that lack of the diagnostic ear-marks, which we now possess—Argyll-Robertson pupil, Westphal phenomenon—allowed some of these chronic cases to remain undetected.

There are cases which show no tendency to progress but in which a single symptom remains in the ascendency. Such cases were prominent before the introduction of salvarsan and are still met, though the individual symptom is now often favorably influenced by treatment. Among the prominent single symptoms of these cases are the lightning pains, altered bladder function, or ocular paralysis. In occasional cases there may be improvement of a number of symptoms during the early period, while one or two symptoms remain unchanged but are not sufficiently severe to incapacitate the patient. In the cases with a single prominent symptom the progress of the disease may be so slow as to be unnoticed, or there may never be extension. Such a case I have had under observation in a banker who has during 30 years continued at his work with limited paralysis of the left motor oculi, loss of deep reflexes, but without progression, and no evidences of incoördination. Another case with limited optic atrophy and Argyll-Robertson pupils has also been watched over 25 years. The patient is now 70 years of age, has retired from his business, is still active in society and is president of a club, able to be about unassisted with occasional lightning pains as his only troublesome symptom. It is interesting to note that these results were obained before the days of salvarsan.

Occasionally after a period of severe symptoms during the initial stage, with incoördination and sensory symptoms, improvement may follow sufficient to make it possible for the patient to return to his work without the advent of new symptoms during long periods. Such cases, unless they die of intercurrent disease, finally progress gradually and after 25 to 30 years pass through the ataxic to the paralytic stage.

Cases in which *gastric crises* are the prominent feature of the incipient

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stage, with modern treatment are made comfortable during long periods. There are exceptions to this statement, but in the majority of such cases it is justified.

In most cases it is difficult to determine the exact time of the advance from the initial to the second stage, for ataxic symptoms are not uncommon during the first year; and in a number of cases there are, as already suggested, *cycles* during which symptoms may increase followed by improvement and stationary periods. As a rule, the return to the condition which existed before the exacerbation, with or without treatment, is not complete and there is a remnant of symptoms which shows progression of the lesion.

In offering a forecast of the effect of treatment on the separate stages of the disease, I can give only general conclusions, but would refer the reader for detailed information to (*d*) the significance of the separate symptoms on prognosis. The initial stage varies in length and symptoms in different cases. There are tabetics who continue with but one or two symptoms during many years, without noticeable progression; the condition is stationary, uninfluenced by any treatment. There are cases in which there is simply a loss of the patella tendon reflex without severe crises, occasional bearable pains, and some ocular paralysis. Such cases permit the patient to continue at his work without marked inconvenience. The reaction of the separate symptoms to treatment and the tendencies of such cases we consider in connection with the separate symptoms; but the general statement is justified that these cases react favorably, so far as sensory symptoms are concerned.

The cases in which the initial stage includes loss of patella tendon reflex, Argyll-Robertson pupil, lightning pains, analgesias, and paresthesias with girdle sensation, ocular paralysis, and early gastric crises may remain stationary during long periods, but as a rule are slowly progressive. If during the initial stage urinary symptoms are superadded, the chances for control of symptoms or latency are reduced.

Early ataxia during the incipient stage and sudden increase of symptoms is always unfavorable; for it indicates deep involvement in a degenerative process of the postero-external, possibly the cerebellar tract, and this condition is not easily influenced by treatment.

No treatment permanently influences advanced degeneration in any stage; inflammatory changes in the incipient stage may be improved. Improvement does not mean cure, and it is not as a rule held unless repeated injections and interval treatment is continued.

The *examination of the blood and spinal fluid* for the Wassermann reaction and for other characteristic cellular conditions proves of inestimable value for treatment and prognosis during the initial stage.

The careful observation of the effect of the combined salvarsan and mercury treatment of the early stage of tabes proves the urgent need of

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prolonged treatment—repeated injections of sufficient size—before conclusions for prognosis are justified. So far as life is concerned the cautiously controlled treatment is practically without danger.

During the incipient stage in a large experience, we have had no untoward results. Herxheimer in a recent lecture reported 40,000 injections of salvarsan given to 11,000 patients in the Frankfurt Hospital under his supervision without a death, and Dreyfus reports 3,000 intravenous injections in 250 patients with but one serious sequel and that was diagnosticated as meningo-encephalitis with recovery of the patient. Medical literature includes a number of deaths resulting from the use of salvarsan, but these are exceedingly rare during the incipient stage of tabes.

In occasional cases the patella tendon reflex, ocular paralysis, pains, and gastric crises are improved. The most encouraging feature of the treatment of the incipient stage of tabes is its favorable influence on the Wassermann reaction, which after one or two injections passes from the positive to the negative phase and often remains negative during long periods in most cases. Occasionally the treatment during the initial stage causes a positive reaction from a previously negative phase during a limited period.

The most favorable cases are those in which the treatment leads from the positive phase to a persistence of the negative reaction. Less favorable cases are those in which after a limited period, there is a return from the negative to the positive reaction. Most unfavorable are those which in spite of treatment, continue to give a positive Wassermann reaction.

My conclusions concerning the prognosis of the incipient or first stage of tabes based upon modern treatment prove the possibility of better control of symptoms than by the previous methods, and in a number of cases the sensory symptoms and ocular paralyses have been so much improved as to encourage us to believe that they may be permanently relieved by several cycles of treatment. Marcus, Weber, McDonagh report the return of pupillary reflex after salvarsan with negative from a positive Wassermann reaction.

In no single case, however, which I have observed thus far and treated according to modern methods, have I been able to banish the manifestations of the incipient stage sufficiently to justify the belief that the treatment did more than postpone longer than could be done by any previous treatment, the sensory disturbances with—as already suggested—improvement in other directions. It would seem that there is a strong likelihood of control of symptoms during stationary periods by modern methods. Whether we shall be able to prevent the advance to the ataxic stage cannot be decided until our experience has grown and abundant time for observation has lapsed.

Increase in weight and improvement of the general condition is the rule after treatment.

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2. Ataxic Stage.—Treatment has in individual cases improved some of the symptoms of the ataxic stage of the disease. As in the initial stage, so in the ataxic, sensory symptoms have been sufficiently improved to justify the treatment. I have seen patients with both marked and insignificant ataxia, who had been incapacitated by severe crises so much improved by intensive treatment—salvarsan and mercury—as to return to and remain at their work.

Occasionally the *patella tendon reflex* has been strengthened and with added mechanical treatment and resulting education, incoördination became less troublesome. All of these cases require repeated injections at varying intervals if the improvement is to be held. The sensory symptoms while they recur, are less severe. Permanent results are not to be expected.

3. The Paralytic Stage.—Treatment has absolutely no effect in permanently controlling the symptoms of the advanced and final stage of tabes. Dreyfus claims that no tabetic is so far advanced as not to justify intravenous injections of salvarsan.

The treatment of tabes by means of the intraspinous injection of the salvarsanized serum taken from the patient according to the method of Swift and Ellis has been entirely without effect in our cases. My experience with the method is limited, but the pains following were so severe and the results so unsatisfactory that I have no desire to continue the experiment, and do not believe that it offers promise of a favorable influence on the disease. Favorable results are recorded by others; the entire question is still *sub judice*.

Dreyfus offers the following report of his experiences with the salvarsan treatment of tabes:—

Leading Symptom.	Number of Cases Treated.	Materially Improved.	Improved.	Uninfluenced.	Symptoms Increased.
Pains	35	20	14	1	..
Headache, neurasthenia, perforating ulcer, bladder symptoms	9	3	4	2	..
Crises	15	7	5	3	..
Ataxia	18	5	7	3	3
		84 per cent.		12 per cent.	4 per cent.

Dreyfus reports that some cases with advanced ataxia, which before treatment could neither walk nor stand for any length of time, were able after treatment to walk comfortably. Donath reports similar experiences.

Donath's material justified the following conclusions after the salvarsan treatment:

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Pupillary reaction returned in	3 of 28 cases
Patella tendon reflex returned in	1 " " "
Walking was improved in	4 " " "
General improvement was manifest in	18 " " "
Marked gain of strength in	7 " " "
Improved mental state in	9 " " "

The reader is referred to the detailed rules given by Dreyfus for treatment in his full article (see references).

(g) The Prognostic Significance of Separate Symptoms.—The rapid development of several symptoms at the same time during any stage of tabes is unfavorable. Cases in which there are but few symptoms offer a much better prognosis than do those in which there is a multiplicity of symptoms usually dependent upon indiscriminate lesions; these cases show rapid progression.

Occasionally with many symptoms, the patient is advanced into the ataxic or from the ataxic to the paralytic stage and falls into a latent but helpless condition in which he may remain during a number of years; or there may be some improvement of one or more symptoms, but not sufficient in the presence of advanced ataxia to return the patient to usefulness.

There are many cases which advance to the paralytic stage after steady progression of symptoms in which the ataxia is almost complete, in which the pains cease and the ocular paralyses remain. The mind is usually clear and active in these cases. I have one such case under observation of a man aged 60 who has been in the paralytic stage over 10 years and who is daily wheeled in his chair to his office, where he presides over a large institution as its president; there has been no apparent progression of the process during the past 5 years. In this case the bladder function has been paralyzed over 12 years; catheter life has been well borne.

Multiplicity of symptoms does not always signify rapid progression: there are occasional exceptions. Collins' experience justifies the conclusion that cases in which the sympathetic nervous system is involved—including crises, trophic disturbances, early troublesome bladder and rectal symptoms—offer the most unfavorable prognosis. With perforating ulcer, arthropathies, and other trophic changes, restitution to the former conditions is unusual.

I have called attention to the cases in which gastric crises have yielded to modern treatment and there is a strong probability, basing our conclusions on the result of the experiences reported by Drefus and Herxheimer and our own observations, that a favorable impression can be made on many of these cases.

Gastric crises do not of themselves shorten life. One of our cases is still living in the paralytic stage which has never during 30 years passed long periods without gastric crises; on the other hand, it is not impossible for crises which have continued during many years to cease and never recur.

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Benedikt says: "Gastric crises are as favorable for prognosis as is the atrophy of the optic nerve." This extreme statement is not justified, but as Malaise says, it should be accepted to prove that Benedikt saw cases in which early gastric crises were without unfavorable influence.

The GENERAL CONDITION of the patient is favorably influenced by the long intervals between gastric crises. I have seen surprising gain of weight during these prolonged intervals, produced in some cases by salvarsan treatment.

The DEVELOPMENT OF THE MORPHIN HABIT by patients with crises of all kinds has limited the usefulness and lowered the resistance of many tabetics in the past. It is a preventable factor and is usually chargeable to the attendant. Modern treatment will prove of inestimable value, reducing the number of morphinists and alcoholics.

I have in connection with the prognosis of the initial stage and the subsequent general consideration, called attention to the unfavorable influence of disturbed bladder function.

ATROPHY OF THE OPTIC NERVE has seemed to many to have an inhibiting influence on the advance of ataxia. This fact was accented by Benedikt, Gowers, Dejerne, and by Bayley and a host of others. Dejerne contended that a blind tabetic rarely developed the symptoms of the ataxic stage. Bayley found that among 12 tabetics who developed optic atrophy early, the onward march of the disease was inhibited in 9. Collins disagrees with the above conclusions.

Malaise reports that in 73 per cent of the cases of optic atrophy observed at the Oppenheim clinic, it developed in the preataxic stage; and that three-quarters of these cases were followed by latency of the tabetic process after blindness; and that in many cases individual symptoms of ataxia were improved or relieved entirely, including urinary incontinence and lancinating pains. In 15 per cent of the cases the disease progressed *pari passu* with the optic atrophy entirely uninfluenced by the latter. The remnant of cases with optic atrophy advanced gradually to the late stages of tabes. I have seen a number of cases in which optic atrophy was a late development, in which the advanced symptoms of tabes remained entirely uninfluenced.

It may be concluded that the fully developed symptoms of locomotor ataxia as a rule persist when once established; that the early development of optic atrophy is not likely to be associated with other severe tabetic symptoms; that in some cases improvement of these symptoms follows advancing optic degeneration; that the statistics offered by Malaise are approximately correct; that the development of optic atrophy during the terminal stages of ataxia is without influence on the tabetic symptoms.

Mott contends that when optic atrophy develops in advanced tabes, it is usually coincident with the progression of serious brain degeneration (paresis). Of his cases of optic atrophy which included 10 per cent of all

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tabetics, 80 per cent developed symptoms of paresis. This conclusion is not generally accepted. In my experience I have found positive evidences of optic atrophy in 12 per cent of our cases of advanced tabes, but of these only few developed paresis. It must be remembered that Mott's experience deals with hospital and asylum cases, and not with the cases which are met in every-day practice.

Ataxia which develops before the end of the third or fourth year of tabes dorsalis indicates progressive tendencies, but is more favorable for life than when it is among the early symptoms of the initial stage or when it develops acutely.

Schaffer called attention to *tabes inversa* in which the ataxia preceded all other symptoms. The prognosis of *tabes inversa* is more favorable than ataxia which is either acute or develops rapidly in the presence of the usual symptoms of the early stage. From 15 to 20 per cent of all tabetics never develop ataxia.

The influence of scientifically directed and supervised exercises on the locomotion of chronic ataxia—Fraenkel and other exercises—is often encouraging; the improvement is naturally greatest in cases where a sufficient remnant of muscles has escaped the loss of coördination, and by education a degree of compensation is obtained to permit of fair functional ability.

Bladder and Rectum Symptoms.—The rule may be accepted that tabetics who are without bladder or rectum symptoms offer a better outlook than do those in whom there is retention, incontinence, or both. But few cases pass through to the paralytic stage without well marked bladder symptoms. The continuous dribbling of urine may be evidence of retention from an overfilled bladder; in advanced cases it denotes sphincter paralysis as well. The dangers of infection from cystitis are increased by bladder paralyses.

Rectal incontinence is rare without bladder paralysis, and occurs only with advanced tabes. Reference is made in this chapter to cases in which retention has not seemed to influence the disease unfavorably; but such cases to escape complications, demand the cautious use of aseptic methods during catheter life.

Westphal Symptom.—Westphal symptom, or *loss of patella tendon reflex,* is one of the earliest of all symptoms and is likely to continue throughout the disease unless extension to the lateral columns finally causes return and exaggeration. In none of my cases has salvarsan treatment permanently changed the knee phenomenon. The same conclusions are justified in connection with the *Romberg symptom* (swaying with closed eyes) and the persistently present *anesthesias, paresthesias* and *analgesias* of the second and last stage. This has not been the experience of all—as has been demonstrated by the statistics of Dreyfus and Donath, quoted in another section of this chapter.

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The loss of the knee phenomenon should not alone be accepted as an indication of far advanced tabes; changed function does not always indicate destruction and degeneration. Many cases in which there is loss of this reflex, remain stationary or do not advance materially during many years.

Ocular Paralysis.—It is often impossible to correctly determine the nature of the lesion which causes ocular paralysis. In our forecast it is safe to consider most cases of nuclear origin, i. e., central; muscular paralyses are more likely to depend upon central than upon peripheral lesions.

The *Argyll-Robertson* pupil does not often disappear in advanced cases. A number of reliable observers have reported periods during which the light reflex returned after its positive disappearance. Donath found with salvarsan treatment, a return of pupillary reaction in 3 of 28 cases. This is possible in early tabes influenced by intensive treatment, but is not likely in the advanced stages.

In considering the paralyses of the cranial nerves, I dilated on the prognosis of the paralyses of the eye muscles (See Paralysis of Ocular Muscles).

Early paralysis of the ocular muscles in tabes is not often followed by the rapid progression to ataxia. Years (2 and 3 decades) may lapse, with progression so slow under these conditions, that it is almost unnoticed by the patient. *Ophthalmoplegia* may disappear under treatment as may the paralysis of separate muscles; this is true of the early stage only, as a rule. 20 per cent of tabetics have ocular paralysis. *Hypotonia* is evidence of advanced tabes and is a symptom of the paralytic stage.

Impotence.—Impotence, once present, is likely to continue. One-third of all tabetics are impotent by the end of the seventh year of the disease. When impotence develops early in the disease it is evidence of rapid progression; such cases offer an unfavorable outlook.

Incontinence of urine early in the disease, often late, is usually followed by impotence.

In some cases sexual intercourse is impossible because of distortion of the penis, and occasionally hemorrhage into the corpus follows the act. Progression of the disease is likely to be rapid when the tabetic in whom the disease is fully developed is excessive in sexual indulgence.

Emotion, long continued worry, any psychic disturbance which makes a profound impression or is continuous, react unfavorably on the tabetic; under these conditions the progression is often surprisingly rapid. Heavy manual labor always causes increase of symptoms denoting the unchecked advance of the disease.

With some acute cases the progression is so rapid that the patient is promptly plunged into the paralytic stage, having skipped the initial and ataxic periods. If such rapidly advancing cases of acute tabes do become

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stationary, it is only after they enter the paralytic stage. This happens occasionally, but the paralytic stage under these conditions is as a rule shorter than in other cases—chronic *ab initio*.

Perforating Ulcer.—In none of our cases have these trophic changes failed to recur after they were healed or partially healed, when the patient was on his feet much of the time.

Perforating ulcers may not always recur in the same location but as a rule they do, or in the immediate neighborhood. They may form either in the ataxic or paralytic stage. Most of our cases were found in the ataxic stage and in men who were on their feet much of the time. They do not affect life directly, save as sepsis develops from their neglect.

Arthropathies.—Arthropathies are trophic changes in which there are characteristic joint enlargements and destructive, usually non-suppurative changes. They develop during the advanced stages of the disease (oftener in the knee joint) and are beyond control by any known treatment. Our cases of Charcot arthropathies and spontaneous fracture have been far advanced and paralytic; other trophic changes add to make the prognosis bad.

(h) The Wassermann Reaction of Blood and Spinal Fluid.—We have already mentioned the importance of the Wassermann reaction of the blood and the spinal fluid. It must be remembered that with progressive tabes the blood may give a negative reaction, while the lumbar fluid will be likely to give positive results.

With tabes, which is active, there are

1. Increased pressure in the subarachnoid space
2. Phase 1 (Nonne), globulin reaction 90 to 95 per cent
3. Lymphocytosis: 85 to 90 per cent
4. Albumin presence: slight or normal.

With Argyll-Robertson pupil and previous syphilitic infection, without syphilitic infection, without positive subjective symptoms of tabes, Phase 1 is present, albumin+ (occasionally normal), lymphocytosis+ (in most cases, though it may be absent).

Plaut, Rehm and Schottmüller made the positive statement that with negative Wassermann reaction of the lumbar fluid and the Argyll-Robertson pupil, without other symptoms, it may be assumed that the failure of the pupil to react to light (Argyll-Robertson) is the expression of a process which has run its course and is favorable. When with symptoms of locomotor ataxia the four factors above mentioned are absent, this happens (according to Plaut, Rehm, etc.) in 7 per cent, 50 per cent of these cases may be considered to be stationary.

The blood serum of tabetics offers positive reactions in over 70 per cent of cases. The lumbar fluid shows a positive Wassermann reaction in almost all cases of active tabes; with progressive paresis and taboparesis, the reaction is present in practically 100 per cent of all cases.

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The lumbar fluid and the blood therefore offer valuable data for the prognosis of tabes, and during the incipient stage demand repeated tests that the effect of treatment may be watched.

(i) Complications.—The combination of independent specific disease of the nervous system during the existence of locomotor ataxia is possible. GUMMATA OF THE BRAIN have been reported, specific and suddenly arising meningitides, and a variety of other lesions. Each deserves separate study, but all influence the forecast unfavorably. Naturally the rapid conversion of a system disease (locomotor ataxia) into one with far-reaching indiscriminate lesions (dissemination) in brain, cord and peripheral nerves influences the case unfavorably.

Tabes complicated by TRAUMA is usually progressive; its course is more rapid than is the average case, and bladder symptoms are often early and exceedingly troublesome (cystitis, etc.).

ACUTE OR CHRONIC ALCOHOLISM always influences tabes unfavorably. These cases are usually neglected; they suffer from infected bladders, constitutional symptoms are numerous, and brain lesions (wet brain) often cause death. With chronic alcoholism it is safe to conclude that tabes is not stationary, but progression is certain and leads to the terminal stage if the patient does not die of intercurrent disease (pneumonia) sooner than do the non-alcoholic cases.

ARTERIOSCLEROSIS; ARTERITIS; AORTITIS.—Among the most frequent complications of tabes is arteriosclerosis and specific aortitis. In some cases the process in the arteries is rapidly progressive, is associated with *hypertension and nephritis.* It may be safely concluded that arteriosclerosis of the mesenterics with *heightened blood pressure* is a frequent factor in causing the *vascular spasm* which leads to *gastric crises.*

Advanced evidences of arteritis are common in young tabetics. *Aneurysmal dilatations* are also a relatively frequent complication of locomotor ataxia. Osler reports 20 per cent of aneurysms in some series of tabes.

PNEUMONIA.—Pneumonia (croupous bronchopneumonia and aspiration pneumonia) is among the more frequent causes of death of tabetics. Any form of pneumonia in the tabetic is serious: the majority die.

PARALYSIS AGITANS.—My material includes two cases in which locomotor ataxia was finally (ataxic stage) complicated by paralysis agitans, in which the former disease seemed uninfluenced.

BASEDOW'S DISEASE.—Oppenheim mentions Basedow's disease as a complication; we have no similar experience to report.

SURGICAL OPERATIONS.—Tabetics bear surgical operations badly; this is particularly true of those cases in which there is advanced arteritis.

INFECTIONS AND TUBERCULOSIS.—Acute infections and tuberculosis are usually serious in tabetics. They offer little resistance to toxemia, particularly when in the last stage.

ACUTE INVASION OF THE MEDULLA OBLONGATA.—There are occasional

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cases of tabes in which the disease suddenly attacks the medulla oblongata, in which there are at once evidences of *vague paralysis in rapid pulse and hyperpyrexia*: the sensorium is promptly blunted; coma and death may result in the course of a few days. The pathologic conditions are either vascular, degenerative or both. Inflammatory lesions which cause these symptoms are infrequent.

Epileptiform Seizures; Vertigo; Hysteria.—Cases of advanced tabes are occasionally complicated with epileptiform seizures or vertigo. Some have periodic outbreaks of hysteria.

The *epileptiform seizures* are usually associated with *transitory unconsciousness* preceding *mental disturbances* and are followed by a period of *memory lapse*. The attacks are likely to recur, are depressing, often lead to melancholia, and are of grave import.

Vertigo of the labyrinthine type is evidence of progression (See Meniere's disease). It may prove to be a persistent and recurring symptom, or it may never return after one or two attacks.

The hysterical attacks are likely to recur and lead to all kinds of *fears* (phobia) and, at times, *imperative conceptions* in neurasthenic, overwrought and weakened tabetics.

The neurasthenic and hysterical element may predominate during any of the stages of tabes and influences the general condition unfavorably.

Social Status.—The social status of the patient proves an enormous factor in the prognosis of tabes dorsalis.

Poverty, with all of its baneful results, robs the patient of comforts including the necessary scientific nursing, which prevents septic infection in the terminal stages of the disease.

The *psychic element* is a paramount factor: the depression of the paralytic who lives in want exerts an unfavorable influence. Under these conditions there is often rapid progression, exhaustion, marasmus; and in same cases cerebral hemorrhage ends the scene.

Septic conditions, including ascending infection from the bladder (pyelonephritis), are responsible for the death of some paralytics—especially among those who are neglected. Cystitis is one of the leading causes of sepsis.

Neglected cases of those markedly emaciated often develop bed-sores (decubitus); once formed they heal with great difficulty, and may also cause septic infection.

Sepsis.—Sepsis may be either acute or chronic. Chronic cases are associated with progressive loss of weight, increasing anemia, albuminuria, irregular fever, and persistently rapid pulse. These symptoms may persist during a number of weeks or months, during which the patient gradually wears out and usually dies in coma, with all of the symptoms of profound toxemia.

The *acute cases* of sepsis are at times foudroyant, or they may lead to

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death after from 7 to 21 days, including delirium and most of the symptoms of the chronic type.

Hemorrhagic Conditions.—*Purpura* has been a terminal condition in some of our cases in which the patient gradually failed, was exhausted, and had been bedridden during varying periods.

The forecast is always unfavorable when hemorrhagic symptoms, increasing marasmus, and bladder symptoms are associated in the ataxic or paralytic stages.

Cerebral hemorrhage in patients with arteriosclerosis is a frequent cause of death; some remain hemiplegic during varying periods.

The *trophic changes* including more particularly perforating ulcer and spontaneous fracture do not lead to death directly, but they often aggravate existing conditions: at times the ulcer causes septic infection; with fracture of the femur bed-sores form which, with persistent cystitis, are complicated with sepsis and death.

Duration.—It is difficult in any case to foretell its duration. No figures which we can give are absolutely reliable nor are they of great importance. There are cases which cover 3 and 4 decades, others in which death follows after between 10 and 20 years, and still other cases in which the disease, because of complications, ends early. Each case demands separate consideration.

Tabetics often reach old age. v. Malaise's records prove that 51 per cent of his cases died after 60, and 83.3 per cent lived to reach 50 and longer.

General Conclusions.—The *degeneration* which characterizes tabes provokes changes which do not permit the conclusion, with our present knowledge, that they can be overcome; in other words tabes dorsalis which presents symptoms sufficient to make its recognition positive, does not, in spite of statistics to the contrary, lead to *restitutio ad integrum.* Symptoms may improve or during periods be entirely absent, but the ravages of the disease continue.

Chronicity is the rule. Long periods of *latency* are to be expected, and often the relief of many sensory symptoms by modern treatment is positively attainable; but persistent and almost continuous attention to the individual case, with scientific nursing, is necessary to hold the patient in the bettered condition.

The **outlook** so far as the life of the patient is concerned is not so bad as is generally supposed by the lay world—a fact which we have accented in this chapter.

Statistics are materially influenced by many factors; foremost among these are heredity, diathesis, social status, occupation, and habits. The wide difference in the conclusions of different observers is demonstrated by the study of the following data taken from leading French and German sources.

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Pellugaud and Faure, Belúgon and Faure, quoted by Oppenheim, report:—

Tabes arrested in	19	per	cent	of	cases
Tabes with remissions in	40	"	"	"	"
Benign in	59	"	"	"	"
Tabes progressive in	30	"	"	"	"
Tabes acute in	6	"	"	"	"
Tabes grave in	36	"	"	"	"
Tabes regressive in	5	"	"	"	"
Tabes cured in	5	"	"	"	"

v. Malaise on the other hand is more conservative and does not speak of cured tabes.

He reports of 76 cases:

2 cases *without symptoms.*
26 " returned to work.
30 " show steady progression.
18 " rapid progression with bad general condition from the beginning.

Syphilis of the spinal cord offers a less favorable prognosis than does cerebral syphilis. The latter is unquestionably always recognized in its incipiency, the former only after a period of progression.

Taboparesis

Taboparesis is a combination of disseminated changes in the spinal cord, brain, and peripheral nerves in which there has been, as a rule, a considerable period of tabes dorsalis with Argyll-Robertson pupil, characteristic behavior of the reflexes, ataxia in some cases, and lightning pains, to which the mental symptoms of paresis are added.

Reverse conditions may prevail, and the symptoms of tabes are added to those of paresis; in rare cases the symptoms of both tabes and paresis are present together from the beginning.

Optic atrophy with tabetic symptoms and even insignificant evidences of mental disease with the characteristic reactions of the lumbar fluid, including positive Wassermann reaction, with or without positive reaction of the blood serum, is strongly suggestive of approaching taboparesis.

We know of no case in our practice in which any form of treatment has favorably influenced the disease. Whether the salvarsan-mercury treatment will ultimately prove of value in those cases in which the diagnosis can be made in the incipient stage of the disease, cannot be decided at the

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present time. Whether such treatment will prevent this late manifestation of tertiary syphilis entirely, cannot be determined until years of observation have lapsed.

General Paresis

(*Dementia paralytica, Progressive paresis*)

General paresis is always due to syphilitic infection: the presence in paretics of the Treponema in the brain, the positive Wassermann reaction of the blood and withdrawn cerebrospinal fluid, as well as the other characteristics—chemical and cellular—of the fluid, positively prove the pathogenesis of the disease.

Five per cent of syphilitics develop paresis. While many paretics were insufficiently treated during the initial and secondary stage of the primary infection, it may happen that thoroughly treated syphilis leads to paresis. Oppenheim and L. Meyer report cases which developed after the salvarsan-iodin and mercury treatment.

The disease is most frequent between the thirtieth and fortieth year; rare before the twentieth and after the sixtieth; as tabes, it is also more frequent in men than in women. In over 20 per cent of paretics, symptoms of tabes dorsalis preceded the onset of mental deterioration.

The same factors which predispose syphilitics to tabes are largely responsible for the development of paresis. I am impressed by the frequency of paresis in syphilitics who are subjected to long mental strain and overwork, and lean strongly to the theory of Edinger, to which reference was also made in considering tabes.

The *average duration* between the initial specific infection and the development of paresis is between 10 and 25 years.

It does not matter what the psychic symptoms are, whether the disease is recognized early or late, what the behavior of the reflexes, however characteristic the pupillary reactions, what the changes in speech or penmanship, whether tremor is present or not, whether paralytic conditions are complete or incomplete—we are absolutely powerless in positively diagnosticated cases to influence the disease itself favorably by any known treatment, though periods of apparent improvement and remission are not uncommon.

The foregoing statement is based on my own experience with the disease, with the full knowledge of the cases of improvement and cure which have been reported by able authorities. Among these I refer to Dana and to the recently published statistics of Browning and Mackenzie and those cited by Oppenheim in considering the literature.

Dana reported a number of recoveries and improvements in whom the diagnosis of paresis had been made. Browning and Mackenzie report 12 of 58 paretics improved, of which number 6 returned to their occupations.

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There are a number of cerebral lesions of specific origin which are not true paresis, but in which the symptoms of paresis are simulated. In such cases improvement or cure is possible, and almost all of the cases reported as cured paresis belong to this class.

It is not uncommon for the spinal fluid of paretics to show a reduction of lymphocytes after salvarsan injections and some have reported improvement of symptoms (Millian and Levy-Valensi).

Remissions and long periods of latency are noted, but the disease finally proves to be progressive. It is these periods of latency or remission, sometimes surprisingly long, which delude the enthusiastic advocates of a good prognosis to believe that the process is stayed or cured.

Jacobsohn says that "the possibility of a cure has a more theoretical than practical value, and in offering the prognosis it need not be taken into account."

"In spite of this fact, it is not wise for the physician to give an absolutely bad prognosis at once; the withholding of the prognosis is wise until all doubt of the diagnosis has been overcome, for every neurologist has met cases in which the progress of the case has proved the possibility of error, and nothing is so humiliating to the diagnostician as to have delivered a death sentence in a case in which it was not justified."

The Wassermann reaction of the blood is positive in 100 per cent of paresis. The withdrawal of the cerebrospinal fluid shows

1. Increased pressure in the subarachnoid space; besides this
2. Globulin reaction (Phase 1, Nonne) positive in from 95 to 100 per cent
3. Lymphocytosis in 95 per cent
4. Wassermann reaction positive by the original method in 85 to 90 per cent, by the newer method in 100 per cent
5. The total albumin content is increased, but varies materially without known cause. The average (Plaut, etc.) is 0.045 per cent, and is greatest in cases which have existed about 1 year.

The cellular elements are greatest in cases which are in their second or third year, and may be reduced by salvarsan (Plaut).

The stage of the disease does not influence the Wassermann reaction of the fluid. The weaker reactions (Wassermann) are found in cases which progress slowly or remain stationary during long periods. Negative reactions are found during stationary periods and remissions. In a few cases salvarsan weakens the Wassermann reaction of the spinal fluid; in rare cases it may become negative.

Trophic changes may develop during the course of paresis, including perforating ulcer, spontaneous fracture, arthropathies and gangrene, and an atrophic condition of the nails; these conditions are but little influenced by treatment.

The majority of our cases have died of cerebral hemorrhage after the usual apoplectic symptoms, which continue two or three days.

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Paretics may become hemiplegic or confirmed epileptics with distinct auræ—*grand or petit mal.*

Transitory paralyses and aphasia characterize some of the cases in the last stage. These paralyses may disappear promptly or continue one or two days. Paretics with advancing paralysis or ataxia, finally become bed-ridden and helpless. They develop bed-sores, cystitis, and sepsis, unless well nursed. Death with septic symptoms in these cases is the rule with marked *inanition.*

Dementia is prominent before the end of the second or third year in the average case, disturbance of speech is fully developed, the facies characteristic, locomotion usually much disturbed, and the sphincters are paralyzed (incontinence of urine and feces).

Death in the second or third year is the rule; acute cases may run a short course, ending within a few months—most of these are hemorrhagic. The cases which live during many years are usually women with marked dementia, senile patients, or taboparetics.

Intercurrent infection has been followed by the remission of symptoms. Steiner reports erysipelas, and Foerster typhoid fever, Oppenheim pneumonia and profuse suppuration closely related to remissions.

Intercurrent pneumonia is often a cause of death in paretics with bulbar symptoms (aspiration pneumonia).

Salvarsan has been used long enough to prove that it does not cure nor materially influence paresis. The only hope lies in the possible prophylactic efficiency of the drug, by its intensive use during the early stages of syphilis.

Ehrlich and his disciples have an abiding faith in the possibilities of prophylaxis from salvarsan; the reported development of paresis after its use by Oppenheim and L. Meyer is discouraging. Time and persistence will ultimately decide the question.

Collins has recently placed himself on record as follows:

"No matter how vigorous or drastic the antisyphilitic treatment, no one has ever been able to say that a case of tabes or general paresis has been cured by it; but, in making this "susceptibility to therapy" a distinguishing feature between the two classes of diseases (the syphilitic and so-called 'parasyphilitic'), we have often lost sight of the fact that the former is a disease of the supporting or interstitial tissue and the latter of the parenchyma, that is, of the nerve elements of the central nervous system. The parenchymatous cells have no more, and indeed no less, capacity of regeneration than the parenchymatous cells of any other organ of the body. Then, so far as we know, there is no substitution of function of the cells of the central nervous system. We are not in a position to say that if one cell in the central nervous system be destroyed, its function can be taken up by an adjacent cell."

"Since the introduction of salvarsan, and its utilization in the treat-

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ment of syphilis, there has been a great amount of reliable evidence—some of which I have furnished—tending to show that the parasyphilitic diseases can at least be brought to a cessation of activity by the appropriate use of this agency. It can no longer, therefore, be maintained that the so-called parasyphilitic diseases progress despite every treatment."

Juvenile Paresis.—Juvenile paresis is due to congenital syphilis and is more frequent in girls than boys.

Rondonis and Strausslers have considered the developmental anomalies in cases of juvenile paresis, and Strausslers found these most prominent in the cerebellum. Strausslers in his work, claims that hereditary syphilis may cause paresis after the thirtieth year.

Salvarsan improves the general condition of juvenile paretics; the Wassermann reaction becomes negative, but soon returns to the positive phase; metabolism seems to be improved. The mental state is not changed.

The reactions of the blood and cerebrospinal fluid of juvenile paretics run parallel with those of the adult. The prognosis is unfavorable.

2. Congenital Syphilis

Heredity in Syphilis.—Our views with regard to the heredity and mode of transmission of syphilis from parent to offspring have been materially influenced by the newer methods of diagnosis.

It may now be assumed with certainty that the disease is conveyed by the mother to the child through the placenta (maternal transmission), and whether the mother presents symptoms of syphilis or not, she offers a positive Wassermann reaction. This disproves the contention of Sir Jonathan Hutchinson that "the father may infect his offspring (the mother never having suffered), and that this is by far the most frequent mode by which the disease is transmitted." In the mother the disease may be latent—she may never develop active symptoms—but she is nevertheless syphilitic.

The mothers of congenitally syphilitic children are immune to syphilis; they cannot be infected through the syphilitic child nor in any other way (Colles-Baume law)—which is another proof of maternal and latent infection; further the same syphilitic child can infect its nurse through the nipple, etc.

For prognostic purposes it may be held that a father who has had syphilis need have but little fear for the safety of his children, so long as his wife shows a negative Wassermann reaction (Bayly). The rigorous treatment of the mother during pregnancy may result in the birth of an apparently healthy child. Most of these children give positive Wassermann reactions and are therefore latent syphilitics. Such children are as a rule immune to syphilitic infection (*Profeta Law*). Unquestionably a large number of these cases which with a positive Wassermann reaction are to be considered latent syphilitics, account for the late manifestations of the

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disease in the subjects of congenital lues which offer unfavorable forecasts (*syphilis hereditaria tarda*).

Not all children of a syphilitic mother inherit syphilis. There are cases recorded in which with twins one was syphilitic, the other escaped infection. Bayly quotes the results of Wassermann reactions of congenital syphilis as follows:—

In 20 cases he found 95 per cent positive. Noguchi and Kaplan in 37 cases found 95 per cent positive. Hoehne found 88 per cent positive. Marcus in 29 cases found 90 per cent positive. Boas in 72 cases found 100 per cent positive.

A parent with tertiary syphilis may show active symptoms and objective signs, and yet the children may be non-syphilitic. Hutchinson says: "a child may wholly escape under circumstances apparently full of risk."

The severity of the infection in the child is not in proportion to the severity of the symptoms in the parent. Mild symptoms or latency in the parent are often found with malignancy of infection in the child.

The subject of congenital syphilis who lives beyond the dangers of the first few years of life offers a good prognosis so far as life is concerned; but he is under par as a rule until he has gained his full growth and often after he is handicapped in the race, and to the expert presents stigmata which brand him.

Characteristic Manifestations.—The syphilitic may come into the world with *grave lesions of one or more vital organs*: kidney, spleen, liver, pancreas, thymus, lung, etc. Specific change in one or more of these may cause death in utero.

Early PEMPHIGUS SYPHILITICUS is usually fatal; this may be present at birth, or develop within a few days.

CHANGES IN THE NAILS AND SKIN are characteristic of congenital syphilis (*onychia syphilitica.*)

CORYZA, persistent SNUFFLES, with crusting in the nose and degenerative changes in the nasal septum, are among the earmarks of congenital syphilis and may persist during early childhood.

GROWTH, NUTRITION AND MENTAL PROGRESS are materially influenced by congenital syphilis. "Fournier's infantilism" characterizes many of these unfortunates.

We have already considered the changes in the LIVER AND SPLEEN, to which we refer the reader. Most of these complications lead to early death.

NOSE AND EARS.—Extension of disease through the nose to the ears is frequent and damaging, often leading to deafness.

ENLARGEMENT OF LYMPHATICS, persisting during long periods with anemia and malnutrition, rob the child of resistance and make him ready to yield to acute infection.

ANEMIA OF CONGENITAL SYPHILIS.—The anemia of congenital syphilis is of three types: (1) chloranemia with leukocytosis (2) pernicious

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type, (3) leukemic type (Bayly). Most forms resemble the usual secondary anemias of infancy and make satisfactory recoveries. *Lymphocytosis* is characteristic of all forms of syphilitic as well as the non-syphilitic anemias of early life. The leukemic type offers the most serious prognosis. There are many nucleated reds, and in some cases the combined count of lymphocytes may be high, reaching 50,000 to 60,000 (lymphocytes, myelocytes, and polymorphonuclear leukocytes).

PNEUMONIA is particularly fatal in the subjects of hereditary syphilis during the early years of life.

Early and late PURPURA may be of specific origin. The hemorrhage of the newborn when specific is usually fatal (*syphilis hemorrhagica neonatorum*).

HUTCHINSONIAN TEETH (notched, malformed, undersized) are characteristic of congenital syphilis. We have never seen these teeth (permanent teeth) in subjects who did not present other positive stigmata of hereditary lues.

EYE LESIONS may be either early or late. *Keratitis* (phlyctenular and interstitial) is frequent and often rebellious to treatment with great tendency to relapse. In many of these forms of corneal inflammation there are permanent though insignificant opacities of the cornea.

CHANGES IN THE BONES of hereditary luetics are frequent; during fetal life the epiphyses may be involved and loosened with cartilaginous proliferation. Most of these are stillborn (*osteochondritis syphilitica*).

Hereditary lues is very likely to interfere with the growth of bone tissue and retards the closure of the fontanelles, or occasionally it happens that there is an abnormal overgrowth of bone which causes premature closure. Such skulls are often congenitally malformed.

Most CONGENITAL HYDROCEPHALUS is of specific origin and offers an unfavorable prognosis. When these children live, as they sometimes do for several years, their development is exceedingly slow and their mental condition is always defective.

Congenital lues predisposes to RACHITIS.

With hereditary syphilis ARTERIOSCLEROSIS OR ARTERITIS is frequent during early life, and may lead to the same far-reaching organic changes which accompany non-specific arteritis. These luetics are constantly on the edge of a precipice: they rarely live beyond the thirtieth year.

When syphilitic babes develop INTESTINAL LESIONS they offer but little resistance and rarely recover.

DESTRUCTIVE DISEASE OF THE SKIN, NOSE AND THE SOFT PALATE is rarely found in cases which receive appropriate and early treatment.

NERVOUS SYSTEM.—The ravages of hereditary syphilis as they are found in the nervous system often lead to irreparable damage. Paralysis, convulsions, epilepsy, blindness, deafness, idiocy are among the dreadful sequelæ of the infection. Fournier includes amblyopia, myopia, nystag-

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mus, asymmetry of the face, congenital heart defects, harelip, spina bifida hydramnion hypospadias, abnormalities of the hands and feet.

Congenital syphilis is uunquestionably responsible for a large number of so-called neuropathies. General paresis may develop in congenital syphilitics; also tabes and multiple sclerosis.

There is scarcely an organ which may not show the ravages of hereditary syphilis; on the other hand it is encouraging to note that the permanent lesions of syphilis are in the majority of cases prevented by timely treatment.

Syphilis can be transmitted to the third generation. This is the concensus of expert opinion, though there are able syphilographers who deny the possibility. Groups of such cases have been reported in medical literature by reliable observers (Fournier). England's greatest authority, the late Sir Jonathan Hutchinson, remained a strong opponent to the views of Fournier.

Syphilis and Marriage

The consideration of this subject requires but little time or space, if we divorce ourselves from sentiment and base our recommendations on scientific and clinical experience.

I may be criticized for this arbitrary rule from which I claim there should be no exception, but in practice it offers the best prognosis. My rule is as follows: *No syphilitic should marry unless he has been radically treated; has shown repeated negative Wassermann reactions during at least two years, and has been without mucous patches for at least twelve months. A single negative Wassermann reaction after treatment is of no value in the matter of prognosis in connection with marriage, if considered apart from other features of the case, and will prove misleading and disastrous.*

Dreyer reports cases in which the Wassermann was negative for 3 or more years, with return to a positive phase and activity of the disease.

Syphilis and Life Insurance

No applicant who has had syphilis deserves to be considered a first-class risk. The dangers of late manifestations, metasyphilitic and cardiovascular complications must be taken into account before giving a rating.

In considering the problems connected with life insurance and syphilitic subjects, it is well to remember that some luetics remain free from symptoms during many years, who suddenly develop active syphilis in its most malignant form.

The average syphilitic will not live to his full expectancy.

Mortuary records show that *diseases of the circulatory organs* are the cause of death in over 50 per cent of syphilitics. The *involvement of the nervous system* is among the frequent causes of death with which life insurance companies must reckon.

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Placing syphilitics in a class by themselves it is safe to conclude that with evidence of prolonged treatment, the period of freedom from symptoms and the negative Wassermann suggested in the rule given above, which justifies the marriage of the syphilitic subject, the risk may, with such added rates as are made by most companies, be accepted.

The Fate of Syphilitics and their Children

Kaufman has followed a large material which made it possible to offer valuable data concerning the fate of syphilitic couples and their children:

It has been found that in 15 to 20 per cent the marriages of syphilitic couples are sterile; 32.9 to 40 per cent of tabetic wives are sterile.

Following 10 couples, all syphilitic, and their children, the following facts were established by Kaufman-Wolf:—

5 of the 10 men died, the causes of death and their ages were:

1. Locomotor ataxia, aortic aneurysm; age 52
2. Pulmonary tuberculosis with heart lesion; age 36
3. Pneumonia with delirium tremens, arteriosclerosis and coronary disease; age 45
4. Insane (suicide); age 36½
5. Paresis; age 57.

Conjugal Nervous Lesions.—In 4 couples the following conditions were found:

	Husband	Wife
1.	Paresis	Locomotor ataxia
2.	Paresis	Delirium tremens
3.	Psychosis (manic depressive)	Insane (psychosis)
4.	Paresis	Paresis

In syphilitics the duration of married life was found between 6 and 25 years. Among 9 syphilitic couples there were 66 pregnancies; these included 33 abortions or stillbirths and 33 living children. Of the 33 living children, 20 died—14 during the first years of life: 3 suicided (12½, 20, 28 years respectively), two were epileptics (both died in public institutions), and one aged 40 died as the result of an intestinal lesion requiring a surgical operation. Thirteen are still living of whom only 2 are normal; all the others are mentally and morally defective. 4 children of the second generation are normal.

All statistics prove the frightful mortality among the offspring of syphilitics during the first seven years of life.

Fournier reports 18 syphilitic families with 161 pregnancies, of which 137 were stillbirths—85 per cent.

Hyde reports 1,121 syphilitic births, with 916 deaths during the first

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year of life. The Moscow Orphan Asylum presents 70 per cent of deaths during the first year of life, among 2,038 syphilitic children. Koplik reports 66,537 births, with 2,732 deaths from all diseases during the first four weeks of life in the Borough of Manhattan, of which but 47 are credited to syphilis.

Haskell gives the results of his observations as to syphilitic infection in the conjugal mate and offspring in fifty-five cases of general paralysis in which the presence of syphilitic infection in the mate was tested, and in eighty-six cases of general paralysis in which there was a definite anamnesis concerning pregnancies and offspring. His conclusions are as follows:

"The large number of 38.18 per cent of conjugal mates of paretic patients is shown to be infected with syphilis. In most of these mates the condition courses unrecognized as lues latens.

"A pitifully small number of them ever receive treatment.

"The proportion of these infected mates who later develop paresis appears to be higher than those who receive their infection from non-metasyphilitic sources.

"The number of completely sterile marriages in syphilitic families in which one individual later develops paresis is abnormally high, constituting 32.5 per cent. This percentage is higher when it is the female mate that later becomes a paretic.

"The number of marriages in which repeated pregnancies result only in abortions is likewise abnormally high, constituting in our series 12.7 per cent.

"Of our series of eighty-six marriages 45.3 per cent were absolutely childless.

"Among 167 pregnancies there were forty-two abortions, miscarriages and stillbirths.

"Among 123 living-born children twenty had already died before their eleventh year.

"The number of living children per family is abnormally small.

"A large number, in some investigations reaching as high as 25 per cent, of these children are actively syphilitic.

"An equally large additional number show signs of degenerative physical conformation and psychopathic tendencies without a positive Wassermann reaction.

"Much of all this is preventable."

Carriers of Treponema Pallidum

There are "carriers" of spirochetes who never themselves know that they are syphilitic; thus a man may acquire syphilis during his first marriage or during illicit intercourse and infect his second wife or others,

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without having himself ever had any of the subjective manifestations of the disease.

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II. Malaria

(Ague-Wechselfieber, Paludism, Intermittent Fever, Estivo-autumnal Fever)

Malaria is a specific infectious disease of protozoan origin, due to the entrance into the blood of one of the Hemosporidia or Hemocytozoa of Laveran attacking the red blood-corpuscles of man, in which the parasite undergoes a definite cycle of development. Its sexual phases take place in the mosquito—the Genus Anopheles—which has become infected by biting sufferers whose blood held the gametes of the Protozoa of malaria (*Plasmodium malaria*).

For our purpose we will consider the features of the disease as presented by:

1. Intermittent malarial fever.
   (a) Quotidian type (double infection with the tertian parasite).
   (b) Tertian type (Plasmodium vivax).
   (c) Quartan type (Plasmodium malariæ).
   (d) Irregular intermittent fever.

2. Remittent malarial fever (always due to the Plasmodium precox or falciparum).
   (a) Estivo-autumnal fever (or continued malarial fever).
   (b) Pernicious malarial disease.
      I. Cerebral.
      II. Algid (or gastro-intestinal).
      III. Pulmonary.
   (c) Black water disease (or hemorrhagic malarial fever).
3. Chronic malaria (malarial cachexia).
4. Mixed types of malarial fever.
5. Malarial neuralgia.

The general statement is justified that the *lesions of malaria* are due to the destruction of blood-corpuscles by the individual parasites causing the special type of the disease, and the toxin produced when the organism divides (*segmentation*).

The *pigmentation* in the various organs of the body is in proportion

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to the chronicity of the disease; is due to the plugging of capillaries by the organisms within them.

The *spleen* is uniformly enlarged in all malarious diseases; its size and the organic changes are proportionate to the *chronicity of the disease* and the *neglect of proper treatment.* The same may be said of the *liver* and of the *blood.* The *malignancy* of all malarial disease depends upon the *number* of *Protozoa* and their *resistance,* the *lack of strength and the endurance of the patient.* As a rule, as will be emphasized in the consideration of the separate forms of the disease, even these factors are overcome in most cases by *specific treatment.* Whether the unqualified statement made by Osler: "No infection—except perhaps tuberculosis—compares with it (malaria) in the extent of its distribution or its importance as a killing and disabling disease" is still justified, is open to argument in the light of recent experiences. Immunity is by no means granted by one or more attacks of malarial infection. It has been shown in the tropics, however, that adults who suffered early in life have at times shown greater immunity than others.

1. Intermittent Malarial Fever

The quotidian type is more weakening than the tertian. When double (two cycles within 24 hours) it is depressing, may be associated with febrile albuminuria, but yields promptly to treatment.

(a) Quotidian Type

The larger number of cases are tertian—the cycle of symptoms recurring every other day at the same hour—observing the *periodicity* which is a family resemblance of all forms of malaria. In an experience of over thirty-five years I have never known of a death due directly to intermittent malarial disease treated by quinin, and the deaths reported by others are so few that they offer only a negligible factor.

(c) Quartan Type

The quartan type is exceedingly rare (17 cases in 1613) (Thayer). Its prognosis is favorable; it is however more stubborn than the other forms of intermittent fever.

(d) Irregular Intermittent Fever

The *merging of a tertian* into a *quotidian,* or vice versa, or the development of *double tertian from single tertian* does not change the favorable prognosis. When the fever is "postponed," i. e., the cycle begins later than in the previous attack, it is evidence of improvement, easy and early control. When the fever "anticipates," it may be inter-

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preted as meaning that conditions are less favorable and demand active treatment, which will usually prove efficacious.

Relapses will follow all forms of intermittent malarial disease unless rigorously treated or the patient is removed from the source of infection. *Spontaneous* recovery may follow change of abode.

2. *Remittent Malarial Fever*

(a) Aestivo-autumnal Fever

(*Continued Malarial Fever*)

This type of infection (*Plasmodium falciparum*) is rarer than the intermittent, and more resistant to specific treatment. The disease is less likely to observe the "family tendencies" in periodicity, is therefore given to *irregularity*, is likely to develop *continuous fever*, resembling typhoid—unjustly called by some typhomalarial fever—and if neglected or improperly treated, pernicious symptoms may prove threatening and serious.

The *paroxysms* of the disease are longer than are those of the intermittent fevers In cases which are benign, there is, as a rule, a decided *drop of temperature* during the early morning hours.

Patients may present with marked evidence of invasion of the *nervous system*, the *typhoid condition* becomes puzzling, the *blood examination* clinches the diagnosis and the prognosis at the same time. Unless the pernicious type of the disease develops, the prognosis continues good.

The Estivo-autumnal infection may be *complicated by the tertian or quotidian fever*, both as a rule will yield to treatment, though the period of convalescence may be prolonged and anemia becomes striking. So-called *"dumb chills"* are among the more serious manifestations of the estivo-autumnal type of the disease. In the more severe types—those with pernicious tendencies—the *nervous system* is invaded, *delirium*—muttering or wild—is not uncommon. An *average paroxsysm* is between 20 and 24 hours. In those cases where *mixed infection* with two Protozoa modifies the temperature curve, there may be considerable difficulty in deciding upon the nature of the infection and typhoid may be strongly suspected. The prognosis should be guarded accordingly until treatment and blood examination clear the horizon.

(b) Pernicious Malarial Disease

This is always serious. As a rule the cases have become chronic; there are organic changes in the *spleen* and in the *liver*, the *blood* has been disorganized, and the patient has been robbed of resistance. In some cases there has been nephritis, occasionally hemorrhagic.

Pernicious malarial complications offer the gravest of all prognoses

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in malarial infections. The symptoms are either, (I) cerebral, (II) gastro-intestinal (algid), or (III) pulmonary.

Cerebral Pernicious Malaria.—Cerebral pernicious disease is always serious.

COMA TYPE.—In some cases there is a sudden overwhelming of the nervous system, with final merging into *deep coma after* a period of exaltation, possibly delirium and few gastric symptoms. In the severe cases there may be *irregular labored breathing* (*Cheyne-Stokes*) or it is stertorous There is hyperpyrexia (106°-108° F.), which with rapid feeble pulse tells of the serious condition of the patient and clouds the outcome. In some of these cases improvement may lead to prompt recovery; in others it is soon followed by a repetition or deepening of symptoms, and death. *Second paroxysms* are almost always fatal. Quaife has called attention to cases of this type which have remained in coma during long periods, which finally recovered. One of Quaife's cases (aet. 18) was unconscious during 48 hours—in deep coma—but finally made a full recovery.

Cases of pernicious anemia of the CEREBRAL TYPE may suddenly develop active *mania, convulsions*, symptoms of active or passive *cerebral congestion*—usually the former—resembling meningitis; there may be paralysis (bulbar, aphasia, hemiplegia) with *eye symptoms, amaurosis, cerebellar symptoms,* or even *tetanoid symptoms.* An early prognosis in either of these pernicious types of cerebral pernicious invasion is impossible; it will always require three days of active treatment to reach safe conclusions. In both these types of pernicious fever *the end of the first period does not justify a positive forecast* for there may be a repetition of all symptoms, with increased severity, and prompt death. In the majority of cases recovery follows the first paroxysm.

Algid (or Gastro-Intestinal) Pernicious Malaria.—In this type of pernicious disease the patient has many of the symptoms and the appearance of the cold or algid stage of Asiatic cholera; the condition is serious, and the outlook is often bad. The *pulse* in the grave forms is small, rapid, without character; the *stools* numerous, watery and large. The *extremities* and the entire body are cold. *Cyanosis* with the symptoms mentioned makes the picture of the most severe cases complete. Death as a rule is not long postponed. In some of the *suddenly depleting forms* of algid disease death may follow in from 2 to 4 hours.

A BILIOUS TYPE is occasionally met, in which vomiting, jaundice and other gastro-intestinal symptoms are in the ascendency. Many of these recover.

Pulmonary Pernicious Malaria.—The pulmonary or pneumonic type of pernicious malaria is characterized by symptoms of *edema, congestion,* or *pneumonic infiltration. Heart weakness* may seriously influence the outcome. In some, death follows promptly from edema of the lungs; in

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other cases prompt treatment—rigorous and persistent—leads to happy recoveries.

In all types of the pernicious disease the prognosis is grave in direct proportion to the number of Protozoa in the blood in the interval following the attacks; though, to quote from Thayer: "the disappearance of the parasites from the blood under treatment of itself". . . . ."does not justify a favorable prognosis, for, despite this, the pernicious paroxysm may continue to a fatal termination."

Purpuric complications (purpura hemorrhagica) with any form of pernicious malaria is evidence of malignancy.

(c) Black Water Disease

(*Hemorrhagic Malarial Fever*)

This usually occurs in East and West Africa, the Southern States of America, and in Central America. Some have held that large doses of quinin given to malarial subjects have been responsible for the symptom complex. Those who have had most experience with the disease agree that this is not true, that as Stephens' investigation shows in a study of 95 cases, Protozoa were present in 95.6 per cent of the cases before the onset of hemorrhagic symptoms, and in 61.9 per cent, on the day of the appearance of the disease. Thayer agrees that malarial hemoglobinuria, as found in the Southern States, is not due to quinin. The most reliable data dealing with prognosis are offered by the experiences of the employes along the Panama Canal zone. These prove that quinin as ordinarily administered is not efficacious but its intramuscular injection has proved specific in its effect in almost all cases of blackwater disease. The *mortality* of blackwater fever is between 5 and 10 per cent. *Complete anuria* may persist during long period (48 to 60 hours), and yet recovery follow.

3. Chronic Malarial Cachexia

No thoroughly treated case of malaria develops the characteristic chronic cachexia. Whenever it is found it is evidence of *neglect* or *repeated infection.*

The *factors which influence prognosis* with this condition are: the reduced state of the patient, the marked anemia, the condition of the spleen, associated kidney and liver complications, dropsies with circulatory insufficiency.

The *anemia* has the ear marks of the secondary type; color index is reduced with erythrocytes low, and leukocytes are also below the normal count. There is an increase of mononuclears—lymphocytes—with nucleated red blood corpuscles. The severity, or depth of these changes as shown by microscopic examination, are potent in giving a forecast. It must be

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remembered that in the presence of grave anemia with changes in spleen and other organs, the patient in a favorable environment with specific treatment may gradually lift himself back to health. Cases of malarial cachexia in which the blood picture of pernicious anemia developed have been found to lead to death within a short time. In these cases the megaloblastic evidences of the disease with a white count approaching leukopenia, a large percentage of small mononuclear cells, and no nucleated red corpuscles were found (aplastic anemia) (Thayer, l. c.; Bignami and Diosini; Ewing). Purpuric eruptions and hemorrhages are present with the more serious cachexias, but do not make the prognosis absolutely bad if the patient can be controlled. The evidences of *dropsy* begin to disappear as the anemia is relieved and circulatory balance is restored.

The *chronic changes in the spleen,* enormous *"ague cake"* and *liver enlargement* far advanced, may yield to treatment; and restoration to health with these complications is not unusual.

In the majority of chronic malarial cachexias the patient holds his fate in his own hands, his *recovery will depend entirely on his ability and willingness to remove himself from baneful surroundings and the religious following of rational medical treatment.*

4. *Mixed Types of Malarial Fever*

Reference has been made to the mixed types of the disease in the preceding pages—the merging of one type into another—the infection of the patient with the Protozoa of estivo-autumnal disease and one or more of the Hemosporidia of the intermittent fevers. In all, the prognosis is good. Recovery may be delayed and convalescence interrupted by the development of the fresh outbreak, as a rule of tertian or quotidian fever.

5. *Malarial Neuralgia*

These types of neuralgia frequently met in the United States with or without febrile movements, as a rule observing characteristic periodicity, unquestionably of protozoan origin, yield very promptly to treatment. They *recover* with lowered resistance and evidences of anemia. There is slight enlargement of the spleen, which disappears with recovery.

Complications

Bronchitis, usually benign, is not infrequent and does not interfere with recovery. **Pneumonia** is not rare; its prognosis depends on many factors which will be considered in connection with *pneumococcus infection.* **Dysentery** is a frequent complication of malaria, usually of the amebic type, oftener in the tropics than in the United States, though epidemics of dysentery in Central New York have been found with widespread in-

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termittent fever. In 1879 and 1880 as the New York Central Railroad built its freight tracks around the city of Syracuse, along the marsh, types of both diseases were found which yielded to antimalarial treatment only.

Nephritis.—Both Thayer and B. Rosenstein call attention to the frequency of this complication. Thayer reports 1.7 per cent of 1832 cases examined at the Johns Hopkins Hospital with acute nephritis. The complication is most frequent in the estivo-autumnal form. Most of these recovered. My experience runs parallel with this. I have traced several cases of chronic nephritis to malarial infection.

The other complications, including *orchitis, gastrointestinal disturbances,* end in recovery.

Miscarriages are not infrequent, during some seasons in malaria-ridden districts these have been as high as 50 per cent in the infected pregnant women. The influence of large doses of quinin in producing miscarriage should not be ignored.

Tuberculosis and **malaria** are frequently associated; the association of these infections is likely to influence the former unfavorably.

The few **anomalies of the nervous system** traceable directly to malarial infection are as a rule favorably and promptly influenced.

In no other infection can a prognosis be given with greater certainty in the overwhelming majority of cases, than in malaria; the therapeutic test—the prompt use of the specific—not only allows early and easy prognosis, but at the same time it clinches the diagnosis.

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III. Amebic Dysentery-Amebiasis

Acute Form

Amebic dysentery is *endemic* in the *tropics* and is caused by the Entameba histolytica and the Entameba tetragena; it is more likely to cause *secondary changes* of grave nature, including metastatic abscesses—liver oftenest. There is greater *tendency to chronicity;* there is greater tendency, as already suggested, to *multiple ulcerations* undermining of

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the mucosa (liquefaction) (Councilman and Lafleur), than with the bacillary disease. The graver types show marked constitutional disturbance during the first 2 or 3 days of symptoms. The tongue is dry; abdomen tender, at times tympanitic; great tenesmus; rapid, small pulse; stools numerous and small, at first fecal, then bloody, foul-odored, at times with slough. The frequent stools with tenesmus and rectal prolapse add greatly to the pitiful condition of the patient and provoke exhaustion. Cessation of pain in the last stage of the disease is often a precursor of death; the irritability of the expulsive muscles becomes exhausted so that painful efforts cease and are impossible. The urine decreases in amount in these cases; is heavily laden with indican; albuminous; with hyaline and granular casts. In the acute period almost complete suppression adds an element of danger.

Cases with many of the above symptoms may continue during weeks and months, emaciating until they look like the reconcentrados seen during the Spanish War, and yet they may recover. In these *grave cases* there is some enlargement of the spleen and liver.

The most severe, usually the *fatal* cases, are of the GANGRENOUS TYPE. These patients are apathetic, have the appearance of deep sepsis, as a rule remain conscious, while stools are involuntary; there may be perforation, and if they recover, misshapen and strictured tissues result. Heart weakness, after a long period in which emaciation and exhaustion are extreme, ends the scene in most cases.

Chronic Amebic Dysentery

There is a strong tendency to chronicity in the amebic form of the disease. Subacute cases often continue to cause a modified symptom complex during 4 to 5, or even 6 months after the subsidence of the more painful accompaniments of the first month. With chronic amebic dysentery there is *chronic invalidism, marked neurasthenia,* or in some cases *melancholia, irritable rectum,* frequent stools; the patients are unable to return to the normal level of health, and in this state they live along for many years unless some of the usual complications terminate life.

Periods of improvement, alternation of diarrhea and constipation, encourage these patients to believe that recovery is complete, only to be discouraged by a return to the subacute or chronic state.

Complications

Abscess of the liver is one of the most frequent and serious complications of amebiasis. Abscess may not form for weeks or even months after the initial symptoms. In one case, in New York State, the patient who had a severe amebic dysentery, developed the abscess 6 months after supposed recovery, and was operated 2 months after its development. The

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symptoms which led to its recognition were chills—irregularly distributed—fever and excessive sweating, with anemia and polymorphonuclear increase. Physical signs of limited enlargement of the liver were present. The abscess was single. *Multiple abscesses* of the liver are rare with amebic dysentery.

Unless abscess is relieved by operative treatment—or as occasionally happens, perforation with protective adhesions prevents general peritonitis and escape of pus—death usually results directly as the result of the abscess; or perforation into the lung or pleura (empyema) prolongs the misery and usually causes death. Perforation into the peritoneal cavity with prompt peritonitis ends the scene in occasional cases.

Brain and splenic abscesses may complicate suppurative hepatitis; in all, the prognosis is equally bad.

Other complications which are occasional causes of sudden death are **perforation of the intestine** with **secondary peritonitis, intestinal hemorrhage, pyelothrombosis, and myocardial degeneration.**

The **invasion of the nervous system** includes the same complications as were mentioned in considering bacillary dysentery; **myelitis** is possibly more frequent with amebiasis. The outcome of these complications is the same in both forms of the disease. **Joint complications** offer the same symptoms and prognosis as with bacillary dysentery.

It is difficult to give figures which are to be relied upon showing the approximate *death rate* to be expected in future epidemics of this form of the disease. Epidemics will be better controlled.

The disease is always serious; its *mortality* varies enormously in different countries with different epidemics, is necessarily influenced by complications and sequelæ, as well as by the surroundings and resistance of the patient.

Symptomatic Dysentery

Dysenteric symptoms accompanying acute infections, typhoid fever, puerperal fever, diphtheria, malaria, scarlet fever, measles, and other diseases, always add an element of danger and receive consideration in the separate chapters dealing with the diseases mentioned.

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IV. Trypanosomiasis

(*Sleeping Sickness*)

Trypanosomiasis is a chronic disease, due to protozoan infection, Trypanosoma gambiense, which is introduced into the body by the bite of a fly—Glossina palpalis—characterized by malaise, fever, increasing weakness, loss of flesh, apathy, and somnolence. The Protozoön has been repeatedly demonstrated in the blood of the infected, also in the cerebrospinal fluid.

The disease has existed in equatorial Africa; now prevails to an alarming extent in Siberia, Congo, Uganda, Rhodesia, along the Niger River and upper Nile.

The infected may live many years, while in occasional cases death results during the first 12 months. In occasional cases there may be long *periods of latency*, with simple invasion of lymphatic glands and slight fever of remittent character. These periods may continue from 6 to 12 months, and then follows the *period of continuous symptoms* with the characteristic *apathetic and sleeping stage of the disease.* In the *severe types*, involuntary discharge of stools and urine are unfavorable and presage early death.

Drowsiness from which the patients are easily aroused, passing into coma or increasing slowly from day to day is unfavorable. When coma is deep, death promptly results.

The *blood* offers a few prognostic data.

Suddenly arising cyanosis with polycythemia (6,200,000 per c. mm.) is promptly followed by death.

Sudden increase of existing anemia, as shown by a fall to 2,000,000 or under, is unfavorable. The blood in average cases shows secondary anemia. Just before death the leukocytic count shows marked polymorphonuclear increase, with large relative increase of mononuclear lymphocytes.

Anemia varies in accordance with the severity of the infection; it is a constant factor; the average count of erythrocytes is between 3,000,000 and 3,500,000.

The *prognosis* of trypanosomiasis has been considered by some to have been favorably influenced by the introduction of the newer arsenic preparations, atoxyl, arsenophenylglycin and salvarsan (Robert Koch and Ehrlich). It is doubtful whether the infected ever recover without the flooding of the blood with some one of the arsenic preparations, and the effect of these is still *sub judice.* No patient can be considered cured until it is established beyond peradventure by repeated blood examinations that trypanosomes have disappeared from the blood, and negative auto-agglutination as well as a negative inoculation of the suspected

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blood into susceptible animals has been fully proved. It is held by Low, that the prognosis is always grave, and the disease almost invariably fatal.

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V. Relapsing Fever

(*Febris recurrens—Relapsing Typhus*)

Relapsing fever is due to infection with the Spirillum of Obermeier (1873); is sudden in its onset, the *fever* continuing during about one week, followed by an almost equal *period of remission*, with a *renewal* of the *original symptoms*. The first relapse is usually 1 or 2 days shorter than was the first attack; this may not always be the case. The average cases have but two attacks, though exceptionally there may be as many as five or six. The disease is indigenous to Russia, Poland, some parts of Africa, and Egypt; is rare in America. High temperatures (105° to 106° F.) are not serious.

The *fever* of the separate attacks ends by *crisis* and a *fall* of three degrees below normal, with profuse perspiration; sometimes considerable weakness follows: all of which need not alarm the attendant. Cases are reported in which the fall was as much as 10° F., ending favorably. The *later relapses* are shorter than those preceding, sometimes lasting only 1 or 2 days. During the **period of convalescence** slight elevation of temperature may occur without giving rise to symptoms (subjective), and these do not interfere with recovery. They are either due to weakness or to abortive or rudimentary attacks.

The **prognosis** of relapsing fever is good; most epidemics show a low mortality (4 per cent) (Murchison). Fatal cases are always due to **complications**—either *pneumonia, asthenia, weak heart, preëxisting disease, or alcoholism.* Strümpell insists that some of the fatal cases are due to "wretched nursing." *Deep jaundice* has complicated serious cases. The diagnosis can be easily confirmed by blood examination. I have seen but one case, which was persistent: there were six relapses. The patient was an active priest who had traveled over a considerable distance; the focus of infection could not be traced. His convalescence was slow but complete; his health has been better since the attack; there never has been a return of symptoms. Vickery (Strümpell) reports one case found in Boston.

One attack does not produce immunity; *cleanliness, destruction of the body louse and bedbugs*—the carriers of the Spirillum—will prevent the spread of the disease.

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VI. Leishmaniasis

(*Tropical Splenomegalia, Indian Kala-azar, Infantile Kala-azar, Tropical Sore or Ulcer*)

The protozoa which belong to the Leishman group and which are responsible for leishmaniasis are of three forms, each differing from the other in morphological and cultural characteristics, each developed in flagellate form. These include the (a) Protozoön of Leishman or Leishmania infantum, the cause of (1) infantile kala-azar; (b) the Protozoön described by Donovan as the cause of the type of the disease in India (2) Indian kala-azar and (c) Leishmania tropica of Homer Wright, now considered the cause of (3) tropical sore or ulcer.

The Protozoön to which Leishman called attention (1900-1902) is found in the blood, spleen and bone marrow. Rogers subsequently confirmed Leishman's find and developed the offender in flagellate form. For over three decades the disease has been recognized as a cause of fatal epidemics in India, where adults are mainly affected, while the infantile type of kala-azar has claimed its victims along the shores of the Mediterranean Sea, in Greece, Turkey, Italy, Malta, Sicily, Portugal, Algiers, Tunis and Tripoli. In India it attacks all ages, while the disease as it is found along the coast of the Mediterranean Sea is often of the infantile type, though adult cases are not uncommon. There are *cultural differences* (Leishman) in these two forms of kala-azar parasites; the infantile type is easily grown on the Novy-McNeal culture medium, while the Protozoön of the Indian type of the disease is not easily cultured on this medium. The Indian parasite is readily cultured in splenic blood with citric acid; not so the infantile form (Leishman-Nicolle). The inoculation of dogs and monkeys with the infantile parasite produces the disease (Leishmania infantum), while the parasite Leishmania donovani (Indian Protozoön) gives negative results.

With all forms of leishmaniasis, the parasites infest the spleen, liver, bone-marrow; at times the kidney, lung, pancreas; mesenteric glands and lymphatics generally. The prognosis of the infantile form of the disease is said by Leishman to be better than the adult form or the type prevalent in India. The recognition of the bedbug and the flea in India and along the Mediterranean as the carriers of the Protozoön has led to prophylactic measures in some quarters, but no benefit to the masses has as yet been reported.

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The disease has raged in epidemic form in the colonies of India during many years and has at times claimed as high as 20 per cent of the entire population. The infection leads to secondary anemia, marked splenomegaly, emaciation, and atrophic changes in the internal organs (intestinal mucosa).

The *average duration* is between 6 and 20 months. The period of incubation 20 to 30 days. Acute hemorrhagic conditions—profuse bleeding from mucous surfaces—nose, gums, stomach, intestines and meninges —may lead to sudden death. The blood condition is advanced, and progressive cases show a reduction of the red corpuscles to 1,500,000, to 3,000,000, and the leukocytes to 700 to 1,000 per c. mm. with a marked polymorphonuclear decrease. Price placed the mortality of the epidemic in Assam at 73.6 per cent.

Schilling contends that cases in which the fever becomes continuous offer the most unfavorable outlook.

Rogers found that when the leukocytic count fell below 2,000 per c. mm. the rapid development of the disease was to be expected. No method of treatment used (including arsenophenylglycin and salvarsan) has proved of value to control the disease.

Nicolle has seen but one case of the infantile disease recover.

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B. Bacterial Diseases

I. Typhoid Fever

(*Enteric Fever, Typhus abdominalis*)

Typhoid fever is a general infection due to the Bacillus typhosus (Bacterium typhi) of Eberth and Gaffky.

Modern sanitation and the study of the life history of the infecting agent, have reduced the frequency of the disease, and promise, with the intelligent coöperation of the lay world and the medical profession, to efface it entirely.

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Typhoid Immunity Through Vaccination

The surprising results of *inoculation* with the antityphoid vaccine as reported by Firth, Major Russell of the United States Army, and many others in all parts of the civilized world, are so convincing that it may be positively asserted that the scientific application of data which Russell and Firth have presented, prove conclusively that we possess in the antityphoid vaccine a prophylactic remedy, which in its results is as efficacious as is inoculation against small-pox. As the result of compulsory vaccination against typhoid in the United States Army, the disease has been practically removed. Personal communication from Major Russell and medical literature give the information that during the year 1913 to July 14th, there was not a single case of typhoid reported in the United States Army, as against three cases for every 1,000 men per annum formerly. What this means to the nations of the earth can be readily understood when we consider the ravages of a single epidemic, or point with shame to the criminal loss of life from this disease during the Spanish-American War. Mankind is under an everlasting debt to Major Russell and the pioneers who have worked in this field with such encouraging and profitable results. If prevention of typhoid fever is to be accomplished and its entire picture changed during the few years of education which will be needed to remove sources of infection, there must be concert of action of those who are in charge of our departments of public health and the public—this means a campaign of education in which our profession must take a leading part.

Typhoid immunity continues as a rule about 2½ years after inoculation.

Firth shows that "even after 4 or 5 years—the maximum period of observation—the rate per thousand among the inoculated is, roughly speaking, only one-fourth that of the unprotected troops."

In 1911 among "80,000 persons vaccinated in the army," there were twelve cases of typhoid with one death, due to intestinal hemorrhage; in 1910, six cases appeared among the vaccinated, with no deaths. Without inoculation, there would have occurred "at the prevailing rates of incidence" 250 cases.

We have now had sufficient experience with antityphoid vaccine to conclude beyond peradventure that it modifies the severity of the disease, lowers the death rate and acts as a prophylactic.

To lower the death rate, it will in the future be considered necessary to consider every convalescent from typhoid a "carrier"—a menace to the public—unless he is properly treated and watched. In all these cases inoculation with antityphoid vaccine should be obligatory. It is the best we have to offer in the present state of our knowledge. In all civilized countries there has been a change in the lowering of the mortality due to typhoid infection which is most encouraging. Thus the following table tells its own story:

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MORTALITY DUE TO TYPHOID FEVER PER 100,000 POPULATION.

	1851–1860	1861–1870	1871–1880	1881–1890	1891–1900
Berlin	96	83	62	20.5	5.9
Vienna	221	110	64	13.	6.
Paris	..	67	80	65.	25.
London	..	..	24	19.	14.

In Central New York, cases in which the surroundings are favorable, with rational modern treatment show an average mortality between 5 and 7 per cent. Hospital statistics are less favorable but do not by any means equal the mortality of former years. In my service in a general hospital, the mortality has never during the past 10 years been higher than 10 per cent. In our own country, the United States, we must confess to our shame that in 1910 there were approximately 25,000 deaths due to typhoid fever. Germany lost but 2,856 lives during the same year and offers an apology for that mortality. A search would disclose criminal carelessness on the part of individuals and municipalities in the majority of these cases.

In connection with the consideration of prophylaxis and prognosis, it might be wise for our lawmakers and departments of health to consider the monetary loss associated with these deaths. Such study and intelligent action would promptly change our statistics. Based upon the computation of Biggs, the loss due to typhoid deaths in the United States alone, during a single year, is in the neighborhood of one hundred million dollars.

Factors Influencing Prognosis

The prognosis of typhoid fever is often difficult, and at times it is impossible to offer a reliable forecast in the individual case because we have no gauge which tells of the depth of the lesions, nor their extent; nor can we be certain that the complexion of the mildest case may not suddenly change for the worse because of hemorrhage, perforation or other unexpected complication. We must therefore reason from the influence of separate symptoms, complications, etc., on the course of the disease. All forms of typhoid, however mild, should be considered serious. No acute infection is so likely to change the character of its symptoms as is typhoid. The severity of the third week of the disease may be out of all proportion to the benign character of the previous period. It is generally supposed that the prognosis of typhoid is more serious in hot than in cold weather. The disease is less serious toward the end of an epidemic than at its height.

In some families there is a decided predisposition to the development of the infection.

Enteric fever is unfavorably influenced by pregnancy, childbirth and the puerperal period. Pregnant women are likely to abort. The progno-

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sis is not however absolutely bad in any of these conditions, though the lowered resistance and vitality must be considered.

Morphinists, alcoholics and the subjects of chronic disease bear the infection badly.

The prognosis of typhoid is materially influenced by:

1. The resistance of the patient.
2. The severity of the infection and
3. The character of the complications.

1 Resistance of the Patient

I have already referred to the beneficent influence of antityphoid vaccination. It is an established fact that resistance is heightened by previous typhoid infection, and Russell as well as Kutcher have proved this fact by incontrovertible evidence.

Age.—Clinicians are all agreed that the prognosis of the disease during early life is more favorable than in adult life. My experiences show a mortality of 5 per cent in children; considering my statistics of hospital and private cases I find the mortality between 10 and 12 per cent in the adult. The prognosis during the first year of life is unfavorable. Beginning with the sixtieth year the mortality is surprisingly high, but the disease is rare. The most dangerous period (Fornet) of the disease in women, who show a mortality of 12.7 per cent is between the fifteenth and nineteenth year of life. In men, the mortality in a large number of cases was 11.7 per cent, and the greater number of deaths between the thirtieth and thirty-fourth year. In a material including 11,000 cases of typhoid (Fornet), the mortality ranged between 10.8 and 11.4 per cent. Young, plethoric, obese, and mentally active adults (twentieth and fortieth years of life), offer a less favorable prognosis than do the thin and less active of the same age.

2 The Severity of the Infection

In a small proportion of typhoids the malignancy of the infection is early manifested. There are cases, fortunately rare, nevertheless sufficiently frequent and important to demand consideration, in which without a prodromal period the patient is at once found violently ill, usually after a single severe chill or repeated light chills, with hyperpyrexia and other symptoms of deep constitutional invasion. In some of these, *meningismus typhosus* is an early accompaniment. In children this type is less dangerous than in the adult; with the latter, this *foudroyant type* offers a very grave prognosis. Curschman has called attention to a class of cases in which the infection is so malignant as to present fully developed and severe symptoms during the period of incubation. In all of these types

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in which the early symptoms are threatening, the prognosis is materially influenced by the rapidity of the pulse; and I am inclined to place considerable prognostic value on facial expression, and the mental state of the patient. Cases in which there is *early hyperpyrexia*, which refuse to yield to treatment, in which there are *no marked remissions*, likely to be associated *with cerebral symptoms and rapid pulse*, justify a very *guarded prognosis;* usually die early and are expressive of malignant infection.

Experienced clinicians have repeatedly called attention to the decided *variation in the malignancy* and in the *nature of different epidemics.* In some of these, the cases are uniformly severe, in others the prognosis proves favorable and complications are either rare or if present, mild. These anomalies of behavior we cannot explain. There are epidemics in which the character of the eruption is hemorrhagic and the disease is likely to be severe. This does not, however, always follow, for in central and northern New York during mild epidemics and in isolated cases we have had hemorrhagic skin lesions which made uninterrupted recoveries. *As a rule an epidemic in which the lesions are hemorrhagic offers a less favorable prognosis than does the usual roseola eruption.* However, before reaching conclusions in these cases associated conditions should be thoroughly considered.

Malignant and severe infection is likely to show its effect on the myocardium early. Heart weakness, circulatory insufficiency early, is often attributable to the direct *effect* of *typhoid toxemia* on the heart muscle or to the paralyzing influence of toxins on the spinal centers and vasomotors. With these conditions there is lowering of arterial pressure, rapid and unsatisfactory systolic contraction, and often a lowering leukocytic count. With malignant infections the blood-stream is overcharged with typhoid bacilli, and Schottmüller has demonstrated the persistence of typhoid bacilli in the blood in these cases in large numbers during long periods, while Lüdke and Sturm have further demonstrated to the satisfaction of the German profession that the *severity of the constitutional symptoms in typhoid fever is in direct proportion to the number of bacilli in the blood-stream*, and that collapse is attended with enormous bacteremia. Hence *a count of bacilli* in the blood should prove of prognostic value. Schottmüller's highest count was 202 bacilli in 10 c. cm. of typhoid blood. This comparatively low count was made before the use of bile-agar, which gave Schüffner (cited by Schottmüller), a count of 872 bacilli in 1.5 c. cm., and which may now be depended upon to give positive data in 50 per cent of all cases.

3. The Influence of the Complications of Typhoid

The influence of the complications of typhoid deserves separate consideration, and this it will receive in the following pages.

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Temperature and Prognosis

In a large percentage of cases the *height of the fever* at the end of the first week of continuous symptoms offers a fair index of the severity of the disease in uncomplicated cases. *Typical cases* during the second week of symptoms, with temperature not higher than 103°F., pulse 100 to 110, and respiration not above 24 per minute, may be considered mild, and without complications offer a very good prognosis. In all cases of typhoid fever, a *decided daily fall of temperature,* making it possible for the heart to rest, and reducing the ravages of too rapid oxidation and consequent degeneration, influences the disease favorably. Such patients are able to bear the disease longer and better than do those whose temperature remains continuously high. It is a further fact that with a *remission* daily, higher temperatures are better borne than lower temperatures without decided fall; therefore I would formulate the following rule: *A decided fall of temperature daily, during a period varying from 2 to 4 hours, associated with a corresponding lowering of the pulse, is of decided advantage to the typhoid patient.*

There are cases with indefinite symptoms during the first two and sometimes three weeks of the disease, with *indefinite and irregular rises of temperature,* often not above 102°F., occasionally from 100° to 101°F., in which the agglutination test is long postponed, and in which abdominal symptoms during this period are likely to be absent. These may, before the termination of the disease, present serious features, making the prognosis problematic for long periods. The foudroyant type already mentioned in connection with malignant typhoid, plunges the patient into high fever at once, within 24 to 48 hours, without marked remission.

The pulse is rapid, in some cases tense at first, becoming promptly dicrotic; there is early cerebral invasion, dry tongue, marked subsultus, occasional convulsions in children and young adults, and often opisthotonos with other cerebrospinal symptoms. This type offers a very unfavorable prognosis; the patients die as a rule within the first week, or early in the second week of the disease.

These cases present all of the features of deep toxemia. Most of the patients are robust adults, over twenty and below the 40th year of life. In some of these cases mixed infection has been considered as the cause of the foudroyant and malignant nature of the disease (Port). On the other hand Lenhartz has obtained pure cultures of typhoid bacilli from the blood in these cases without either ulceration or swelling of the intestinal glands. (See Typhoid, without intestinal lesions.)

Prognosis in Various Forms of Typhoid

Protracted Fever.—There are frequent cases—the majority of which are only moderately severe, though a few may be considered severe—in

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which the *fever persists during unusually long periods.* These may cover a febrile period varying from 4 to 6 or even 8 weeks. I have the notes of a case which terminated favorably, in which on the ninety-sixth day of the disease, without known complications and without preceding decided remission, the temperature still averaged 102°F. As a rule it will be found that in these cases the fever is of an intermittent character and atypical. In the majority of these cases the prognosis is favorably influenced by the relatively short or even normal period of continuous fever, and the decided remissions during the longer period of intermittent fever. If in these cases of prolonged fever the digestive organs do not revolt, and there are no other serious complications; in spite of extreme weakness and muscular wasting, full recovery may slowly follow. These cases are likely, after the long postponed afebrile period is established, to have rises of temperature on slight cause. An occasional case of this kind passes beyond the long period of fever, but fails to lift itself from the weakness which follows; wasting continues, the appetite does not improve, the organs of digestion become intolerant, vomiting is often an uncontrollable symptom, the abdomen is abnormally resistant and retracted, and death follows weeks or months after the initial symptoms of typhoid. There is another set of cases in which without known cause a slight fever persists long into the period when full convalescence is expected; which yields promptly, and offers a changed prognosis so soon as the patient is allowed to sit up and move about cautiously. Delafield called attention to these cases years ago.

Abortive Typhoid and Mild Irregular Typhoid (*Typhus abortivus, Typhus levissimus*).—In America we meet but few cases of the abortive types of the disease; that these are occasionally found in the midst of endemics or epidemics we cannot deny. Some of these correspond with the description given by the older writers of *ephemeral fever* (*febricula*). The majority of these cases offer a favorable prognosis. They are all characterized by a *short febrile period.* Liebermeister's classification of these cases as

1. Typhus levissimus
2. Typhus abortivus

is most satisfactory.

1. Typhus levissimus. (*Mild Typhoid*).—In these cases the disease does not seem to be fully developed. The febrile period may be short and mild; one or more of the usual leading symptoms of the disease may also be of short duration, even in the presence of a slight continuous febrile movement. In occasional cases there is a remittent type of fever, in others the curve is irregular and erratic. The pulse in favorable cases is scarcely changed in character or in frequency. The general condition of the patient continues good. The disease ends in recovery as a rule between the fourteenth and twentieth day of the disease, without marked invasion of the sensorium. In occasional cases the early days of a mild typhoid may

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include high fever with other transitory constitutional symptoms, but they soon prove to be benign because of the decided change in the nature of all attending conditions. In the United States cases of this kind such as Liebermeister has described, running their course in from 6 to 8 days, are among the clinical rarities. Mild typhoids may be followed by slow convalescence. The enlarged spleen is in evidence early in most cases.

2. Typhus abortivus (Liebermeister).—Occasionally a free outspoken fever, early, with deep invasion of the sensorium at once—but with a reassuring pulse—runs a short course and may lead either to prompt or to slow convalescence. In these cases the severe headache during the first week, complete anorexia and apathy, occasionally a *single heavy chill and early enlargement of the spleen, are not to be interpreted as arguing against a favorable prognosis.* In these as in all cases of typhoid the pulse (myocardial condition), and the frequency of the respirations offer data which must be given great weight before safe conclusions are justified. In some of these abortive types the fever may return to normal within 9 to 14 days. Most of these cases, however, begin with a decided chill; after a short prodromal period, the temperature rises promptly; there is as a rule some apathy with sleeplessness; there may be delirium; the roseola eruption is found early; but the pulse is likely to continue good. Complications and distant typhoid infections (liver, gall-bladder, lung, heart, etc.) occur, but are less serious and less frequent than with the usual types of the disease.

The light form of typhoid (levissimus) differs from the abortive type in several particulars. In the former the constitutional symptoms are fewer; symptoms referable to separate organs are unusual; the temperature is higher and associated with greater wear and tear in the abortive type; while albuminuria is more frequent, with casts (hyalin, granular, and blood). Roseolæ are fewer and less constant in the abortive than in the typical disease. In both types of irregular fever considered, tympany and diarrhea are not as a rule disturbing. A full consideration of these earmarks will make it comparatively easy to prognosticate in these cases; but it must be remembered that none of these patients is immune to perforation, peritonitis, hemorrhage or pulmonary complications. These added dangers are not frequent. *Relapses* are frequent after the milder types of fever and these may run a more typical course than did the original infection. The prognosis remains uncertain for days following the beginning of the relapse, but usually proves good.

Ambulatory Typhoid (*Walking Typhoid Fever.*)—Most cases of ambulatory typhoid may safely be considered to have been neglected. In these, patients have continued about, in spite of a prodromal stage and a train of continuous symptoms which, in all probability always include some elevation of temperature. The fever in these is not so high as in the usual cases; there is less exhaustion and malaise attending it early; but the picture which is finally presented by these cases is often serious and the

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outlook grave. This is particularly true of those typhoids who have been exposed to the hardships of travel. My experience justifies the conclusion that *travel adds enormously to the dangers* of every fully developed typhoid.

While ambulatory typhoids may present with normal temperatures during the early hours of the day or during almost the entire morning, close observation will show some elevation later in the day. The *pulse* in spite of low temperature or afebrile state is rapid, as a rule, when these patients surrender, and there are often subjective complaints, including palpitation. In hospital cases I have often noticed more or less incoherence on admission. I have learned to give a very guarded prognosis in these cases; they run an uncertain course, are likely to develop grave abdominal complications—endocarditis, pulmonary infarct and infection, thrombosis, abscesses—and what I fear most, degeneration and dilatation of the heart muscle. There are on the other hand ambulatory cases so mild as to give no uneasiness, running a smooth and uneventful course to full recovery.

Afebrile Typhoid.—Cases of feverless typhoid are not frequent; they do, however, occur. They are likely to be found in homes where several typical cases of the disease exist. In some of these the temperature has remained normal throughout, others have shown a slight elevation usually toward night of from ½° to 1°F. In all the diagnosis has been confirmed either by a positive Widal reaction, or by blood cultures, or by both. Without fever, the associated symptoms referable to the abdomen have persisted. Unquestionably a number of so-called *"latent cases"* to which Koch referred, belonged to this class. He held that these cases existed without marked symptoms, were not as a rule reported to the public health authorities, and that they continued to be a menace. The Trier Commission drew attention to the dangers to the public of these cases, and established the fact that the number of infected cases in Trier was nine times greater than the number "sufficiently ill to require treatment." The majority of afebrile typhoids recover: death may follow, as has been reported by Strube and Fräntzel.

In the aged, afebrile typhoid, in the presence of chronic cardiovascular and renal disease, offers but little that is encouraging; in alcoholics and those reduced by previous disease the prognosis is correspondingly bad.

Sudden fall of temperature is occasionally met when not of serious import. It should always be viewed with suspicion and the patient should be carefully observed, that its significance may not be misinterpreted. The fall may presage a favorable termination, for it has been my experience that in a majority of cases in which the true cause of the fall has not been made clear promptly by the development of positive symptoms, there has been a rise of temperature within 12 to 24 hours and then a gradual return after a varying period to normal or, if there are no added complications, with a more or less irregular behavior the fever has gradually subsided. In these cases the decided fall of temperature is not associated with

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the symptoms of collapse due to profuse hemorrhage, nor the pain and physical signs referable to the abdomen which are characteristic of perforation, nor the added evidences of circulatory embarrassment, which occasionally develop suddenly at the height of the typhoid infection.

Sudden effacement of liver dulness with *fall of temperature, abdominal pain,* and *collapse,* is suspicious of perforation and justifies a serious prognosis. Blood pressure study will in the presence of perforation and beginning peritonitis show a slight, but easily demonstrable rise to promptly fall after a few hours, and may prove of prognostic as well as diagnostic value.

Post-typhoid Pyrexia.—Transitory elevations of temperature which may last a short time during the period of convalescence are not of serious import. In some—particularly nervous subjects—excitement, worry, muscular effort, a hearty meal, or errors in diet during this period prove sufficient to cause these sudden rises. Long continued obstipation may also provoke insignificant exacerbations. Hypothermia, persisting for several days, mentioned by Osler, is also without unfavorable influence. In some of these cases the pulse has been erratic, occasionally slow and irregular, in others, abnormally rapid during limited periods.

Circulatory Disturbances in Typhoid

Pulse.—It is fortunate that the pulse of typhoid fever is in most cases slow in comparison with the temperature. In no other long continued acute infection does the heart behave so favorably. *The pulse offers the safest indications for prognosis in typhoid fever.* With a pulse, of good character, and average frequency of 100, in spite of an elevation of temperature of 103° to 104°F., the prognosis continues good. As has already been stated, remission of fever during the day with associated drop in heart frequency is favorable. When the pulse is persistently high, whatever the temperature—if above 120 to 130—there is serious complication, or heart weakness threatens. When the pulse, which during the first two weeks has been reassuring, begins to intermit in the third week, is irregular and rapid with feeble heart sounds, possible dilatation must be considered suggestive of myocardial insufficiency. When, with such a pulse there are evidences of pulmonary congestion or edema, consolidation, or bronchial catarrh, the prognosis is exceedingly grave. *Cyanosis* with evidences of myocardial insufficiency and correspondingly rapid pulse justifies an unfavorable prognosis. *Rapid pulse with deep invasion of the sensorium is of serious import.* Restlessness and insomnia with delirium add to the danger. With rapid pulse (120 to 140) and hurried respirations (30 to 50) the patient must always be considered to be in a serious condition, and search will usually reveal pulmonary, renal, cerebral or other complication, though a tired heart with consecutive stasis may explain the symptom

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complex. *Dicrotism* at the height of the disease, if the heart is not abnormally rapid, is not as a rule unfavorable. There are but few cases of enteric fever in which there is not more or less dicrotism at some time. *Rapid pulse* is the rule with infantile typhoid and does not argue against a favorable outcome of the disease. After the sixth or eighth year of life the character of the pulse and its frequency in children approaches that of the adult.

As the disease advances, *blood pressure* is likely to be lowered and the pulse amplitude correspondingly changed. The pulse is softer and smaller: this is a natural result of toxemia and not unfavorable. Persistence of normal blood pressure is favorable. Increased frequency of the heart with sudden fall of blood pressure is unfavorable. Increase in the frequency of the pulse toward evening, with a reassuring condition during the day does not change the prognosis. In all cases there is likely to be a close relation of temperature and pulse. With a rapid pulse early in the disease whatever the change of blood pressure, unless such condition depends on a neurotic state or the patient normally had a rapid, irritable heart, that organ is likely to prove insufficient.

The *heart* itself is in most cases the seat of interstitial and degenerative changes (myocarditis). The extent of such changes is shown by the weak and muffled systolic sound, mitral systolic murmur—due to relative insufficiency—accented II. pulmonary sound, distant heart sounds—embryonic in character—marked change in rhythm, and in severe cases decided dilatation of the ventricles. The early signs of cardiac weakness are due to vasomotor paralysis; the evidences of myocardial degeneration follow.

Sudden Death.—Approximately 1.2 per cent of typhoids die suddenly from a variety of causes, among these myocardial invasion. Degeneration is the most frequent; thrombosis, embolism, cerebral apoplexy, pulmonary edema—due as a rule to circulatory insufficiency, and renal invasion, degenerative in character—are also to be considered.

A distinct mitral systolic murmur with accented II. pulmonic sound is not of serious import unless there are other marked evidences of heart weakness in rapid pulse, etc. *Diffuse apex-beat* with *rapid heart* is deserving of careful consideration and is, if persistent, indicative of serious cardiovascular disturbance. In many patients, unless the nervous system is profoundly involved, the pulse as counted by the physician is likely to be somewhat accelerated, hence the average count of the nurse must also be considered. *Relatively slow pulse* with dicrotism and normal arterial resistance, or only slightly lowered blood-pressure, is not of serious import. *Sudden increase* in the frequency of the pulse with or without evidences of collapse is always ominous, and will be fully considered in connection with intestinal hemorrhage, perforation and other complications. The *crossing of the temperature curve* by the *pulse curve* is suggestive of increasing danger.

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Bradycardia following rapid pulse, particularly during the convalescent period or in the terminal febrile stage, is not of serious import unless it is an evidence in young or in old subjects of *heart block*. Any *change in the coronaries* or *disturbance of conduction* (*Stokes-Adams*) adds a decided handicap, and materially lowers the chances of recovery.

Accented aortic II. sound with increased ventricular effort and *forceful* impulse, suggest a compensatory effort to overcome *vasomotor paralysis* in the periphery, usually in the domain of the splanchnics, and unless relieved overtaxes the cardiovascular system and leads to cardiac asthenia finally (Ortner). It not infrequently happens that the pulse rate is higher during periods of relapse than it was originally. Every case of typhoid fever during convalescence or after recovery may show some abnormality of function or organic cardiovascular change. Of all modern clinicians, Thayer deserves the greatest credit for having demonstrated the fact that arteriosclerotic changes are unusually frequent in patients who have had typhoid, as well as other functional and organic heart lesions.

Posttyphoid myocarditis may be the cause of symptoms during *convalescence* in which the slightest excitement or muscular effort provokes palpitation or some subjective complaints referable to the heart. These types of myocarditis lead to complete recovery within a few months.

If the pulse is persistently rapid during the period of convalescence with gradual improvement in the general condition of the patient, gain in weight, and good appetite, the heart will after a reasonable period of rest with moderate exercise, return to its normal state. *Rapid pulse* persisting *during convalescence,* without increase of weight, slight evening rise of temperature, general condition below par, must lead to the suspicion of some added infection—possibly tuberculosis, pus deposit, or other *hidden complication.* In severe cases, besides vasomotor paralysis already mentioned, there are anatomic arterial changes (Wiesel) in which the media is involved in a process of atrophy, connective tissue change, and lowered arterial resistance. This adds an element of danger which is overcome in the average case.

Thrombosis.—Phlebitis cruralis.—Thrombosis of the anterior crural is a frequent complication which fortunately as a rule follows either toward the end of the acute fever, or early during the period of convalescence. While it is often exceedingly painful and causes in all cases more or less fever and acceleration of the pulse, it usually leads to full recovery after weeks or months. Occasionally double *crural phlebitis* postpones convalescence. I have never seen a case which led to gangrene, but rarely a detached bit of thrombus has led to fatal embolic infarct. Thrombosis or septic thrombophlebitis may invade any vein, and add a complication of serious import—pulmonary, portal or cerebral thrombosis —fortunately rarely encountered.

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ARTERIES.—Arteries may occasionally be occluded by either an *embolus* or *thrombus.* The complication is rare, not necessarily fatal; it may lead to *gangrene.* Hölscher claims that 1 per cent of all typhoid deaths are due to embolism of the pulmonary artery. Limited superficial losses of tissue due to embolic infarct or arterial change heal slowly as a rule; their prognostic significance depends upon the cause and source of the embolus. If due to *endocarditis,* the latter may prove *malignant* or *septic;* then the prognosis is bad.

GANGRENE.—Gangrene due to thrombosis, embolism, or arteritis may prove serious when extensive. It is not a frequent complication; usually is unilateral, and involves one lower extremity. In all of these cases *associated conditions, sepsis,* and the *extent* and *location* of the process must be considered. Invasion of the iliac, femoral or posterior tibial is most frequent. In rare cases the prognosis becomes absolutely bad because of double symmetrical and far-reaching gangrene (Trousseau, Potin, Mercier, Bachmayr and Dodd). The occurrence of double gangrene is so rare that in an active hospital experience covering over thirty years, not a single case has presented.

Pericarditis.—When positive symptoms, subjective and objective, of pericarditis present, these are due as a rule to septic infection, which is likely to be purulent and which adds a factor of danger to an already serious condition. Hölscher, in an analysis of 2,000 typhoids found this complication in .7 per cent of cases.

Endocarditis.—Endocarditis arising during the course of the disease is not frequent. Occasionally with mixed infection the endocardium has been involved. It requires caution to eliminate in diagnosis the malignant endocarditis of typhoid type but not typhoid fever, in which the prognosis is always bad. In 2,000 typhoid autopsies (Hölscher) there were 11 cases showing acute endocarditis, i. e., .5 per cent.

Disturbances in the Respiratory Organs

Respiration.—The safest indications for the prognosis of a typhoid patient are offered by the pulse (heart) and the respiration (lungs). With a reassuring pulse and no evidences of serious pulmonary involvement or embarrassment of any kind, as shown by hurried or labored breathing, the outlook may in the overwhelming majority of cases be considered favorable. Most serious complications will at once accelerate pulse and respiration.

Rapid respiration without evidences of cardiac or pulmonary involvement, out of proportion to the height of temperature, unless of purely functional origin (hysteria, fear, neurosis) is always suggestive of a serious complication; its true significance can only be decided after its cause has been unearthed. Occasionally diabetes mellitus with acidosis

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in a typhoid subject has been found to be the cause of hurried respirations. In other cases profound toxemia has proved to be the cause without high temperature but with great exhaustion; finally, with rapid heart such patients succumb to the disease.

In the majority of typhoid cases pulse and respiration bear a close relation to the temperature; in a large number of cases however in which the temperature reaches a high degree, respiration is not markedly changed. These are favorable combinations. The cause of rapid respirations in any case determined, the prognostic significance is easily cleared.

Considering *pulse and respiration* together, I would submit the following: *With acute typhoid infection a rapid pulse is always more ominous than a high temperature, but with such complications as pneumonia or mixed infection, hurried, abnormally high respirations are more serious than a rapid pulse. Where the two are present together, i. e., rapid pulse and abnormally frequent respirations, at the height of the acute disease unless one can be sure that the symptom complex rests on hysterical fundament, the prognosis is exceedingly grave.*

Most enteric fevers are associated with catarrhal changes in the upper respiratory tract and included bronchi.

The *ordinary nasal changes* have no influence on the course of the disease, save as the dry mucosa, crusting, and at times ulceration with possible perforation, add to the discomfort of the patient.

Epistaxis.—Nosebleed is present at some time as a rule—usually early—and unless profuse is of no prognostic significance. *Repeated profuse nosebleed* with other evidences of *hemorrhagic disease*, usually with grave constitutional disturbances, often deep involvement of the sensorium, dry tongue, crusting, and sordes on teeth whenever present, is ominous—this symptom complex is not infrequent in chronic alcoholics with typhoid fever.

Catarrhal Pharyngitis and Laryngitis.—Catarrhal pharyngitis and laryngitis do not influence prognosis materially. Deep ulceration of the larynx, with or without edematous swelling are usually found on the posterior laryngeal wall, and often with the more malignant types of the disease. The edema alone may threaten the life of the patient and demands prompt relief, otherwise death follows. When *ulceration* leads to necrosis, perichondritis, cutaneous and deep emphysema, the outlook is bad. The mortality is as high as 40 to 50 per cent (Türck). In occasional cases, deep ulceration with destruction of tissue leads to *stenosis* if the patient recovers, demanding tracheotomy and the permanent or long wearing of the tube. Uncomplicated *laryngeal ulcerations* are not infrequent, as has been proved by post mortem study; they may be present without causing symptoms and in the majority of cases heal permanently, without deformity.

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Bronchitis.—Bronchitis, present in practically all cases of typhoid —when uncomplicated, does not lower resistance or influence prognosis. Extension to the finer bronchial tubes (bronchiolitis) is common in the severer cases, and is therefore of grave import. Consecutive *atelectasia* adds another factor of danger, but unless *bronchopneumonia* (lobular pneumonia) follows, the prognosis, though grave, may yet hold hope of recovery. Disseminated islands (lobular) of pneumonia with atelectasia is a serious complication in all cases, and in all ages.

Hypostatic Congestion.—Hypostatic congestion, usually found in the lower lobes, is serious in proportion to the added obstruction which it offers to the heart—always serious, when extensive—in the presence of a weak myocardium and deep infection. Pneumonic infection of the hypostatic lung, i. e., *hypostatic pneumonia,* is as a rule life-threatening, always a serious complication, and often ends in death (50 per cent). Children rarely develop more than transitory hypostatic congestion, and are not prone to have added pneumonia: this is due to the shorter duration of the disease and relatively infrequent heart weakness.

Pneumonia.—Pneumonia (lobar, i. e., croupous) is a serious complication of typhoid fever. In the larger number of typhoids this complication (Fraenkel-Weichselbaum diplococcus) is developed during the height of the disease, near the end of the fever or during convalescence early—rarely late. As a rule there are early evidences of heart weakness, rapid pulse, and decided lowering of blood-pressure, with characteristic respiration—all of which affect prognosis unfavorably. Cyanosis added to these conditions is serious. My experience with pneumonia in typhoid fever has been exceedingly unfortunate: over 50 per cent of these have died. It is exceedingly rare to find a favorable outcome after the fortieth year of life. Lobar pneumonia complicates typhoid in from 5 to 7 per cent of cases, the lobular form in 8 per cent. There are occasional cases of typhoid in which the early symptoms are clearly those of pneumonia, so-called *pneumotyphoid,* in which the lung may clear, and the patient falls into the continuous and characteristic symptoms of typhoid fever. Invasion of bronchial glands—suppuration—may prove serious, and occasionally leads to empyema. *Strepto- and staphylococcus infection* of the lung with typhoid, mixed infection, including the Bacillus typhosus, causing either lobar or lobular pneumonia, always demands a guarded prognosis. The pure pneumococcus infection offers a better prognosis than does the streptococcus.

Lung Abscess.—Lung abscess is rare. If it follows pneumonia complicating typhoid, gangrene may finally develop, and death is the rule.

Pulmonary Infarct.—Pulmonary infarct may cause hemoptysis; if small, it may lead to no serious condition, but if large or if it causes gangrene and sepsis, or if caused by vegetating typhoid or septic endocarditis, the prognosis is bad. Gangrene has already been mentioned in connection

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with lung abscess and pulmonary infarct. As a rule it is associated with or follows lobar pneumonia, develops late in the course of the disease. An idea of the frequency of gangrene can be obtained from the following figures: Liebermeister in 230 deaths from typhoid found 14 cases of gangrene; Griesinger in 118 found 7; Curschmann—Leipzig statistics—in 228 found 10 cases; Hölscher in 2,000 autopsies of typhoids found 40 cases, or 2 per cent. Murchison considered pulmonary gangrene exceedingly rare, having met the complication only twice. The prognosis is bad.

Pulmonary Edema.—Pulmonary edema arising in the course of typhoid without other pulmonary or cardiac complication is rare, always serious, but not necessarily fatal. Our experiences do not justify the high percentage, i. e., 14 per cent, of this complication as reported by Hölscher. Simple non-tuberculous *serous pleurisy* is not as a rule serious, but it retards recovery if it arises late. It is naturally associated with the pneumonias of typhoid, and as already stated, these offer a serious outlook, depending on conditions mentioned in the consideration of pneumonia as a complication.

Purulent Pleurisy.—Purulent pleurisy, i. e., empyema, complicating typhoid, usually following pneumonia, may under some conditions prove serious. The prognosis depends on many factors: time of complication, resistance and general condition of patient, time of recognition, ability to relieve by prompt and thorough drainage. *Bloody and foul effusions* with typhoid are always indicative of malignant infection.

Pulmonary Tuberculosis.—It has been the experience of most clinicians that associated tuberculosis of the lung with typhoid is due to the awakening of latent tuberculous disease which antedated, as a rule, the acute infection. If the process is of the acute miliary type it may be difficult, if an early complication, to differentiate without blood-culture and agglutination tests. In *all cases of miliary tuberculosis complicating typhoid, the prognosis is unfavorable.*

Limited tuberculous deposits, i. e., infiltrating tubercle without disorganization, which have been lighted to activity by the typhoid process, under favorable conditions and environment, may yield to treatment and a return to latency.

Pneumothorax.—Pneumothorax (pyopneumothorax) I have never met in connection with typhoid. It is an exceedingly rare complication. In the reported cases it was dependent on some one of the conditions (pneumonia, tuberculosis, etc.) mentioned, and the outcome has been fatal.

The Blood

The blood offers some data which may serve in the prognosis of typhoid fever. The *albumin and iron content* of the blood are reduced in proportion to the severity of the disease. *Fibrin* is also below the normal unless

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it is increased by complications, such as disseminated bronchitis and pneumonia. In most cases of typhoid a moderate anemia gradually increasing as the disease advances is the rule, and not unfavorable. Thayer, Winter, and Curschmann have shown that in the average favorable cases there is during the first days slight *reduction in the number of red corpuscles;* with young powerful men, this is less marked than in women or in the weak. The former give an average count of four million, the latter three million. The reduction continues until the end of the febrile period and during the early days of convalescence. Then the rise begins in favorable cases, usually in 2 to 3 weeks.

The clinician is not to be discouraged if the normal count is slowly reached; this is the rule. Relapses may give lower red counts than were found with the original fever, and yet the prognosis remains unaffected. Hemoglobin in the average favorable case does not sink far below 70 per cent. *Sudden anemia* is suggestive of intestinal hemorrhage.

The *leukocytic count* is of considerable value. The tendency in typhoid fever is toward low leukocytic counts—possibly the first day of the disease and of relapses excepted—when it may reach 10,000. The average count in adults during the first stage is from 2,800 to 4,500. The more serious the infection the lower the count. Leukopenia must be expected in typhoid fever (85 per cent). The period of convalescence finds the patient with a normal count.

Neutrophilic leukocytes are increased during the first days of the disease, but as the symptoms increase in severity the count of these falls as low as 1,000 to 2,000. With improvement, when the patient is fever-free there is an increase, a gradual return to normal; often the count mounts above the normal (Schottmüller). There is prompt disappearance of *eosinophils* from the typhoid blood. *Return of eosinophils is an encouraging feature; as a rule this indicates convalescence.*

There is a progressive decrease of *lymphocytes* during the active period of fever; their return, like the return of eosinophils, is favorable.

If with complications such as pneumonia, intestinal hemorrhage, perforation, diarrhea, pus accumulation, and nephritis (acute), marked leukocytosis is absent, particularly *neutrophilic leukocytosis,* prognosis is unfavorably influenced, because, as Schottmüller has suggested, there is an inability of the bone marrow to react. The following are safe *conclusions* for prognosis:

The persistence in typhoid blood of even a few eosinophils is a favorable feature. Relatively high neutrophilic values without complications are also favorable. Increase of lymphocytes argues in favor of a decline of fever. Marked leukopenia, particularly a low lymphocytic count, is unfavorable. With the complications already mentioned low leukocytic counts argue in favor of serious conditions. Blood counts alone should never lead to positive prognosis for there are cases in which in spite of severe

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leukopenia, that is, low values, patients have made full recoveries.

In considering the malignancy of typhoid infection we called attention to the fact that the disease is severe in direct proportion to the *number of bacilli* found in the blood stream and that a *count of bacilli* in the blood was of great prognostic value (See references to Schottmüller's and Schüffner's experiences).

Disturbances of the Alimentary Canal

The Mouth.—The organs of digestion offer valuable prognostic data. In serious cases the LIPS are abnormally dry, crusty, and often cracked and bleeding. In favorable cases, the lips are moister, with less evidence of change. In unfavorable cases, there is associated dryness of the mouth; the buccal mucosa is materially changed, ulcerated and bleeding, with sordes on teeth; gums incline to bleed. As a rule with these changes there is a dry tongue, covered with a thick brownish dirty coat, red at the tip and shining. The above picture, with marked *fibrillary twitching of the tongue*, is usually associated with cerebral invasion and is found in the more serious cases. Such conditions early, argue in favor of a severe course of the infection.

The TONGUE is changed in practically all cases, and its study is often a valuable prognostic index. A *dry cracked tongue*, slowly protruded, long exposed, returned only after repeated suggestion, with apathy or muttering delirium, is characteristic of severe deep toxemia and is serious. *Moderate fibrillary twitching of the tongue* is present in almost all cases and is not of serious import—less significant if the tongue continues moist and the patient is free from the symptoms of deep infection. The severer cases show the greatest fibrillary twitching of the tongue; in these the nervous system is profoundly invaded, as is shown by active subsultus tendinum and other symptoms. *Moist tongue* is found in the milder cases of typhoid with few mouth and lip lesions and with clean teeth or little sordes.

There are cases in which changes in the *tonsils* are so evident as to cloud the diagnosis. Unless these are gangrenous or diphtheritic or are associated with noma, they are soon accompanied by the symptoms of general typhoid disease and do not influence prognosis. The more serious but rare complications are, as mentioned, diphtheria, deep ulceration, and noma.

Parotitis.—Parotitis whether suppurative or not is always a serious complication. It is added as a rule when the patient is weakened by the toxemia and other complications; is always febrile; may occasionally be double. There is in these cases the added danger of *thrombosis* (jugular and cerebral), *phlegmon, infiltration* of surrounding muscular tissue, *peri-*

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chrondritis, and *facial paralysis*. Parotitis complicates from .3 per cent to 1 per cent of typhoids, and of this number one-half die.

Stomach Disorders.—An intolerant stomach is always a decided handicap. *Persistent vomiting* from whatever cause lowers vitality and reduces the patient's chances. When this continues, and remains uncontrolled in the third and fourth week, with *anorexia*, the wasting is enormous; the pulse grows smaller; the tissues are dry; and death is the rule. Persistent vomiting is at times an early symptom of added *meningitis;* then it is "propulsive" and associated with other positive symptoms. Sudden severe vomiting with pain, not due to error of diet or transitory disturbance, is suggestive of *perforation, peritonitis, latent hemorrhage*, or *involvement of the appendix*. I have seen two cases in which after convalescence was fully established, *uncontrollable vomiting*—the cause of which was never cleared—with increasing consecutive weakness, caused death.

Tympany (*Meteorismus*).—Absence of tympany is always favorable. Severe cases at their height are likely to be burdened by intestinal distention. It is a burden, for it increases the work of the heart, displaces organs—the liver more particularly—and adds to the patient's discomfort. Suddenly arising tympany with evidences of collapse is significant, for it may mean serious complication, *perforation, adynamic paralysis, hemorrhage*. Early meteorism is not usually significant. In many cases proper diet will prevent or control it, if not, then it must remain a factor in prognosis.

Modern clinicians view tympany more as an expression of general infection (intestinal paralysis—adynamic) than an index of the extent of the intestinal lesions.

Diarrhea.—In a moderately severe typhoid in which the bowels are loose the average number of stools is from 6 to 10, many of these are finally found with serious complications referable to the intestines. Movements above this average (ten) denote a serious condition. *If most passages are involuntary and other symptoms are correspondingly severe, a guarded prognosis is justified. Frequent involuntary passages are always of grave import.*

In my hospital and consultation practice I have found at least one-third of all cases free from diarrhea during the entire course of the disease. *Occasional frequency* of evacuation is more favorable than *persistent diarrhea*. Constipation does not affect prognosis unfavorably. Those epidemics have seemed to be least malignant in which the intestinal symptoms, more particularly diarrhea, are fewest. In some epidemics the number of constipated patients outnumbered those with diarrhea. The depth and number of intestinal ulcers do not always bear a close relation to the severity of the typhoid toxemia.

Intestinal Hemorrhage.—Intestinal hemorrhage complicates from 4 to

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6 per cent of all typhoids. The frequency of this complication varies with different epidemics. *Slight admixture of blood*, during the second and third weeks of the disease, is not serious, and is not as a rule followed by larger losses of blood. Women are less likely to have severe and large hemorrhages than men. Curschmann reports the days of occurrence of hemorrhage in 148 cases observed by him as follows:

6th to 9th day	12
10th to 12th day	23
13th to 15th day	23
16th to 18th day	31
19th to 21st day	17
22d to 24th day	9
25th to 27th day	11
28th to 30th day	10
31st to 33d day	3
34th to 36th day	4
After 36th day	5
	148

The *prognostic significance* of intestinal hemorrhage with typhoid fever depends very largely upon the time of its occurrence, the condition of the patient, his resistance, the condition of his heart, and the quantity of blood lost.

Different individuals react differently under similar conditions to the loss of blood. There are typhoids who may be thoroughly depleted, in whom the pulse becomes thready and exceedingly feeble, and blood pressure and pulse amplitude materially reduced, who for some unknown reason promptly regenerate sufficient blood to keep them alive during the critical period, the disease leading to full recovery. With *high fever, previous rapid pulse, deep involvement of the sensorium*, added *intestinal hemorrhage,* and *marked tympany,* a picture is presented as serious as any, save that of perforation, which we meet in the course of the disease. Patients are better able to bear hemorrhage the nearer they are to the end of the febrile period. *Hemorrhage during the early days of typhoid* (ninth to the fourteenth day), if profuse or if repeated in the presence of other grave symptoms, *is always serious*—more serious if the patient is corpulent and in middle life. There are occasional cases which are influenced favorably by moderate intestinal hemorrhage (Graves, Trousseau).

Relapses are not often complicated by intestinal hemorrhage. Children are not often found with this complication; this is due to the fact that the ulceration is not so deep as in the adult. Naturally, *the more*

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frequent the bloody stools, the greater is the danger. Sudden death due to intestinal hemorrhage is rare; in most cases repeated bloody stools during several days deplete the patient. However, in occasional cases patients are carried safely over the critical period following large hemorrhages with associated symptoms, only to die after relatively small losses of blood from the intestines later, when the attendant had reason to feel fairly secure. *The prognosis in all cases of intestinal hemorrhage should be guardedly given;* the most experienced clinician can offer no positive forecast; there are always days of anxiety and uncertainty in the presence of this complication.

When death followed hemorrhage in cases which serve as the basis for conclusions in this chapter it was between the fourth and seventh day as a rule—in a few cases between the ninth and fifteen day. My percentage of deaths due directly to intestinal hemorrhage is not above 20 per cent, but as already hinted different epidemics offer a different mortality. There have been epidemics in which 50 per cent of the patients with intestinal hemorrhage died. Homolle gives 44 per cent, Griesinger 31.2 per cent, Liebermeister 38.6 per cent. In our own country Osler gives a series of 829 cases, with blood appearing in the stools in 50, or 6 per cent. Of these 5 cases died, or 10 per cent. The same author gives a series of 118 cases of hemorrhage with 12 deaths, or 10 per cent, and a series of 131 fatal cases with 12 deaths from hemorrhage. He states again (ref.) that hemorrhage occurs in 7 per cent of all cases.

Peritonitis.—Peritonitis either circumscribed or diffuse, from whatever cause, always secondary, is one of the most serious complications of typhoid fever. *When due to perforation of an intestinal ulcer* we consider it the *most fatal of all complications* (perforative peritonitis).

Perforative Peritonitis.—*Time of Occurrence of Perforation.*—In 73 cases Curschmann found that perforation occurred as follows:

On the	11th	to	20th day.....	23
	21st	to	30th day.....	31
	31st	to	40th day.....	13
After			40th day.....	6

Perforative peritonitis among children is rare. *It matters little which portion of the small intestine is the seat of perforation, or what the size of the opening, the dangers are the same and death is the rule.* Perforation is found in 3 per cent of typhoid fevers. Statistics vary between 2 and 12 per cent. In men the complication is more frequent than in women. *No case of typhoid, however mild or severe, is free from the possibility of perforation and consecutive perforative peritonitis until the ulcers have been fully healed, the cicatrices are strong, and the peritoneum*

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over the ulcer has been fully protected by nature's reparative process. This means complete recovery.

Prompt death with symptoms of perforation in collapse, with characteristic facies is the rule unless the condition is recognized within the first hour or two after its occurrence, and is relieved by immediate surgical interference. I am fully satisfied that in occasional and exceedingly rare cases, perforation takes place and general peritonitis is prevented by previous localized peritonitis and plastic organized protection. Such a case has been described in which death finally resulted from hemorrhage, and the autopsy clearly showed the earlier perforation (Elsner). The possibility of *perforative appendicitis and peritonitis due to typhoid ulceration of the appendix* should not be forgotten. In these cases the *early diagnosis* with rational radical surgical treatment offers the only hope.

Perforative peritonitis due to *rupture of the spleen, gall-bladder, suppurative mesenteric glands, or abscess of the liver* is serious but offers a slightly better prognosis, if diagnosticated early, than does intestinal perforation.

Liver and Bile Passages

Pathologic research has demonstrated the frequency of invasion of the liver, more particularly the bile passages, in typhoid fever. Jaundice is not a frequent symptom. Hölscher found it in 1.1 per cent, 22 cases in 2,000 of those who died of typhoid. *Previous diseases of the gall-bladder, cholelithiasis, typhoid cholecystitis or cholangitis, acute yellow atrophy of the liver, and abscess,* are among the causes of jaundice with typhoid.

Jaundice.—Jaundice may in occasional cases be due to destructive blood changes—an evidence of malignancy when it is associated with hemorrhages from various organs—hematuria, albuminuria, myocarditis, and coma; and death follows promptly as a rule.

Typhoid infection of the bile passages and gall-bladder in individual cases is not to be ignored as a prognostic factor; its importance has increased during the past decade.

Cholecystitis.—Cholecystitis may be present without causing symptoms or in any way influencing the immediate prognosis of the disease but there can be no doubt of the fact that it serves as a cause of subsequent disturbances, more particularly *gall-stone formation;* 30.9 per cent of Curschmann's cases of typhoid fever followed during long periods, presented symptoms of gall-stones after the original infection.

Animal experimentation strengthens all conclusions which tend to demonstrate the importance of typhoid infection as a cause of gall-stones. It is a clinical and bacteriologic fact that *the Bacillus typhosus finds a suitable habitat in the gall-bladder and bile passages,* and often remains there undisturbed during long periods. Thus, in considering the question of the

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prognosis of these cases, we are not to forget the dangers of these carriers (Futterer, Chiari, Flexner).

The Skin in Typhoid

Roseola.—The number and location of the roseola spots have no bearing on the prognosis, so far as I have been able to conclude from my experience. The depth of color does bear a direct relation in many cases to the severity of the infection. Thus a mottled skin, with dark, at times hemorrhagic skin lesions is expressive of malignancy.

Miliary Eruption.—Miliary eruption, sudaminous in character, is found in most cases and is not significant. Often the *sudaminæ* are most abundant after the profuse perspiration following a decided fall of temperature, and are therefore favorable.

Bedsores.—Bedsores are not frequent and as a rule are evidences of faulty or insufficient nursing. In occasional cases their formation cannot be prevented; this is true of those with deep invasion of the sensorium, frequent involuntary discharges of feces and urine, and at times myelitis. When bedsores are a *late complication* they heal as a rule but slowly, may cause some fever and other constitutional symptoms. When *early* they are usually an expression of deep infection or lack of resistance, and do not argue in favor of a mild typhoid. *Bedsores with deep bone involvement are ominous.*

Abscesses.—Abscesses of the skin, superficial or deep in the subcutaneous connective tissue, are late complications, and simply retard recovery, without interfering with full recovery unless an expression of *pyemia* or other constitutional or *mixed infection.* When one of the latter complications has caused multiple abscesses, the prognosis remains clouded for days at a time; in most cases recovery is slow, but many die for want of resistance and because of the deep infection.

Alopecia and Atrophic Changes.—The lesions referable to the *nails and hair* are late manifestations without prognostic significance. *Alopecia and atrophic changes* are rarely permanent, and mend slowly after several months.

Purpura Hemorrhagica.—Purpura hemorrhagica with skin lesions—*macules or large ecchymoses*—occasionally arises during the period of convalescence. *Hemorrhages from one or many mucous surfaces* may reduce and deplete the patient. **Hematuria, intestinal bleeding, severe epistaxis, and bleeding through the external auditory canal** are frequent accompaniments of typhoid purpura. The prognosis in most of these cases is good in spite of extreme anemia and weakness. Recovery is very slow. *Simple purpura hemorrhagica* should not be mistaken for the bleeding and cutaneous lesions due to *malignant endocarditis—hemorrhagic infarct*—which offers a grave prognosis, as do those forms of cutaneous and other

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internal hemorrhages complicating typhoid, due to deep blood changes, disorganization, septic conditions and pernicious toxemia. *All hemorrhagic lesions of the skin influence prognosis,* and demand serious consideration. When purpura or any hemorrhagic cutaneous lesion is due to *nephritis,* either acute or chronic, the prognosis in most cases is bad.

Erysipelas.—Erysipelas, an occasional early or late secondary infection of the skin is, when complicated with deep meningeal symptoms, serious—more serious when early. *Limited erysipelatous blushes,* without marked constitutional disturbances are not of great prognostic significance.

Phlegmons depend, in their importance for prognosis, on location, extent, the severity of the associated symptoms, time of occurrence, and other accompanying lesions.

The Spleen

Enlargement of the spleen, which is present in 90 per cent of typhoid cases, offers but few data which are of use in prognosis; its diagnostic value is much more important.

The spleen often decreases in size after severe intestinal hemorrhages. *Sudden decrease in the size of spleen* after hemorrhage is evidence of marked depletion and is ominous. *The size of the spleen bears no relation to the severity of the infection.* The spleen recedes as the disease spends its force. So long as the spleen remains enlarged the disease has not run its course. *Enlarged spleen persisting* without fever, does not justify the conclusion that the patient is free from the possibility of relapse.

I called attention to the serious nature of *rupture of the spleen* in connection with the consideration of peritonitis as a complication.

Complications causing changes in the enlarged spleen are comparatively rare. In 577 autopsies of typhoid patients made by Curschmann at Hamburg and Leipzig, he found the following changes in the spleen:—

Infarct and hemorrhage	25	times
Abscess	4	"
Rupture	2	"
Perisplenitis	16	"

The Genito-Urinary Organs

During the febrile period of typhoid fever the *urine* is reduced in quantity and concentrated, as in all acute infections. The increased intake of fluids is not likely to have a marked influence on the quantity secreted at the height of the disease. Typhoids who during the febrile period secrete *satisfactory quantities of urine* may be said to add a favorable factor to the symptom complex. During convalescence there is often a decided increase in the quantity secreted, and this is favorable.

Urea and uric acid loss, increased during the active period of the dis-

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ease, *is lowered as the patient improves and returns to normal during convalescence.* Severe cases show the presence of *leucin and tyrosin,* though Frerichs and Stadler claim these are present in all cases.

Return of normal chlorid excretion reduced during the height of the disease, is favorable and is found early during convalescence.

Albuminuria.—The albuminuria of typhoid fever may be either:

1. Febrile Albuminuria
2. Albuminuria of Nephritis
3. Albuminuria due to other complications

1. Febrile Albuminuria.—If all cases are cautiously followed albuminuria will be found in at least 50 per cent; in most of these it has no influence on the course of the disease. In some, however, it is of great importance. In all cases *the presence of albumin* demands scientific differentiation, that its prognostic significance may be fully determined.

Those cases in which febrile albuminuria is of *grave import* show its presence *early;* in these it is likely to persist, and the *quantity large.* Almost 30 per cent of these die, as against 10 per cent—the average mortality of the disease. Curschmann places the mortality at 25 per cent. *Mere traces of albumin* without other symptoms are to be numbered among the benign febrile albuminurias.

Febrile albuminuria which develops *toward the end* of the febrile period is *serious* and demands close inspection to determine its cause. Febrile albuminuria may disappear, to reappear later, and is likely to accompany exacerbation of other symptoms. The microscopic picture of febrile albuminuria ought to include only *few hyaline casts*—no others—*uric acid crystals, urates, few squamous epithelia and white blood-corpuscles.* If there are many hyaline casts and other elements, i. e., renal epithelia are increased, the prognosis is influenced thereby, and in all likelihood there are organic changes in kidney substance. *Urobilinuria* with febrile albuminuria is suggestive of liver changes.

There has been so far as we could find in our cases, no relation between *indicanuria* and the severity of these cases of febrile albuminuria; the *presence of indican is not to be considered dangerous.*

2. The Albuminuria of Nephritis.—It is often impossible to differentiate febrile albuminuria from that of nephritis in typhoid fever. It has been my experience that *acute nephritis* is not a frequent complication of the disease. Curschmann reports its presence in 4.87 per cent.

Gubler and Robin originally described a symptom complex which is now characterized as *nephrotyphoid,* in which the symptoms, more particularly the urinary picture, of *acute parenchymatous nephritis* are in the ascendancy.

These cases during their early history are often mistaken for uncomplicated nephritis, but they are not as a rule difficult of recognition. They

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are not all serious, and most do not develop uremic symptoms, though occasionally patients have died of nephrotyphoid with profound uremia, but as a rule without the usual edema of acute nephritis. My experience with typhoids in which the diagnosis of nephrotyphoid was justified, has been favorable. Four cases seen during the past 20 years all recovered. In most of these cases the urine is more or less bloody. There are a number of recorded cases (Immerman) in which death resulted with the full complement of symptoms of nephritis, hemorrhagic and non-hemorrhagic, at the height of the typhoid process.

In the majority of such cases the urine is red, bloody, contains large quantities of albumin, many casts (granular, hyalin and blood), abundant red blood corpuscles, and epithelia.

These cases are further characterized by deep involvement of the sensorium, and by the presence of but few or no abdominal symptoms of typhoid. It is not wise to consider these cases other than the usual typhoid infection, in which there is parenchymatous degeneration of kidney substance, in which, however, the symptoms of such change for a time at least, are decidedly in the foreground. *Whatever the symptoms, whenever typhoid fever is complicated by an acute parenchymatous nephritis, it adds an enormous element of danger, clouds the prognosis, and it may be assumed that the nephritis is a part of a profound toxemia; never an independent disease.* Death follows in between 40 and 50 per cent of typhoid nephritides during the second week, with all of the symptoms of deep infection. These patients do not as a rule become uremic. The larger number of fatal nephritides which I have seen complicating typhoid have been positively hemorrhagic. When they recover there is not likely to be any remnant of nephritis, as is customary after scarlatinal nephritis.

Hemorrhagic infarct of the kidney associated with typhoid from whatever cause (endocarditic, embolic, thrombotic), is always a grave disturbance.

In *children* the result of painstaking examination of urines has demonstrated the fact that *a limited number of red blood-corpuscles is normally present in the urine*, and further, that albuminuria is not so frequent as in the adult—all of which adds to the factors which make the prognosis of typhoid in children favorable.

Postfebrile nephritis is not frequent; most cases which I have seen finally recovered or became latent. Occasionally patients have developed, after several months of albuminuria with casts, general dropsy and heart complications, and have died either of uremia or with symptoms of dilated and worn-out heart.

3. Albuminuria Due to Other Complications.—*Cystitis* is a cause of albuminuria; it may prove annoying but does not of itself threaten life.

Typhoid bacilli are present in the urines of all typhoid patients in large numbers (one hundred million in a single cubic centimeter) a fact

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which adds an element to be seriously considered in prophylaxis and in prognosis.

Pyelitis is rare, though Schottmüller calls attention to its occurrence, and in his case found typhoid bacilli in the urine months after full recovery.

Albuminuria may be present with many *complications of typhoid*, such as *pneumonia, pleurisy, empyema, meningitis, otitis, erysipelas, kidney abscess* and other conditions in which its prognostic significance must of necessity depend largely upon many factors, most of which have been considered in this chapter.

Neither the *Ehrlich diazo-reaction* nor the more recently considered *Russo reaction* to methylene blue have much bearing on prognosis. The former is found in 90 to 100 per cent of typhoids, the value of the latter is still *sub judice*; our figures are not yet sufficiently reliable to justify consideration. I am satisfied that for diagnostic purposes it will never displace the Ehrlich test. It would seem that serious cases as they improve, often lose the diazo-reaction. Genken holds that the reaction is coincident with the period of Eberth bacteremia, the appearance of the bacilli in the blood, and that it is lost as these disappear. With *relapses the reaction returns* if due to Eberth bacteremia, not if due to other complications; hence under these conditions *it is of diagnostic and prognostic value.*

It must not be forgotten in considering the significance of the *Ehrlich diazo-reaction* that it *is present with acute miliary tuberculosis, cerebrospinal meningitis, lobar pneumonia and measles.*

Orchitis.—Orchitis, a late complication of but few cases, ends in full recovery and usually without suppuration.

Menstruation.—Menstruation during the course of the fever has been present in the majority of cases but once, and has occasionally been premature, without influencing the symptoms so far as I could judge. Menses usually appear when due during the first 10 to 14 days of the disease, not as a rule, when due later, until some time after the period of convalescence has been fully established, and they are then without untoward results to the patient. Menstrual anomalies following typhoid need not disturb the patient; the flow will, after a reasonable time, return to its previous regularity. *Acute suppuration of the vulvovaginal gland, catarrhal conditions of the genitals, moderate local edema, decubitus, i. e., vaginal ulcers,* only prolong convalescence, without threatening the patient.

Gangrene of the Vulva.—Gangrene of the vulva I have never met in my practice. Spillman and others, Hoffman and Liebermeister included, have reported cases and consider the complication fatal as a rule.

Pregnancy.—Pregnancy, as already mentioned early in the chapter, adds to the dangers of typhoid infection. A large proportion of pregnant women abort (46 to 56 per cent), usually during the second week of the disease, though this accident may happen later. *Once beyond the febrile*

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period, the chances are against miscarriage. Murchison considered the prognosis of the pregnant woman with typhoid as very serious. Most authorities who have recorded their experiences place the mortality between 8 and 16 per cent.

The Nervous System

There are but few cases of typhoid which run their course without symptoms referable to either the

1. Central nervous system, or
2. Peripheral nervous system.

1. Central Nervous System.—The bearing of symptoms referable to the central nervous system on prognosis is exceedingly important. *The forecast is less favorable in direct proportion to the depth of cerebral invasion, as shown by positive symptoms and by lumbar puncture.* The prognosis is particularly bad when in adults, full-blooded and previously healthy, these cerebral symptoms persist. Liebermeister places the mortality of these cases at 70 per cent. There is a class of cases which has been characterized as *meningotyphoid, meningismus typhosus,* in which the early symptoms are those of meningitis, the typhoid manifestations appearing later. These patients may present all of the appearances of fully developed meningitis, including the Kernig symptom, opisthotonos, vomiting, hyperesthesia, and wild delirium at times, sometimes low muttering delirium. As a rule these symptoms clear with the appearance of a train of continuous typhoid manifestations. Persistence or increase of these evidences of deep cerebral (meningeal) invasion must be interpreted as signifying a serious condition. *In children, meningismus typhosus is* more frequent than in the adult and is less serious.

Cerebral manifestations are most likely to be present and characteristic in moderately severe cases with the beginning of the second week. The so-called *typhoid condition gives a clue to the severity of the individual case.*

Wild delirium at night beginning in the second week, repeated during the day at intervals, with more or less rigidity, exalted reflexes, dry tongue, sordes, high fever, correspondingly rapid pulse, retention of urine, Kernig symptom, mind clouded, with characteristics in the lumbar fluid of purulent meningitis, with or without typhoid bacilli, is a complex of symptoms of enormous gravity, but not absolutely hopeless.

Alcoholics, with symptoms of *wet brain, alcoholic meningitis,* with *active delirium,* always justify a grave prognosis. *Involuntary discharges of urine and feces* are symptoms of the more serious typhoids.

The *temperature* in cases of serious cerebral invasion is not necessarily high; in some it is but slightly elevated and these often drag a long and monotonous course during many weeks before the sensorium is entirely clear, while occasionally they lead to psychoses, which require attention

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during many months. More serious and permanent mental disturbance may finally develop.

Active, persistent subsultus tendinum is an expression of the more serious types of the disease; as is *picking* at the bed-clothes and imaginary objects.

Convulsions, in very young children, are occasionally an early symptom in cases with high temperature or in those of neuropathic habit, but are not of serious import as a rule.

Improvement or moderate control of nervous symptoms by baths and other treatment is always a reassuring experience. *Psychoses* when present during the febrile period are likely to disappear early during convalescence and as a rule do not return. In some cases delusions, hallucinations, illusions, or obsessions persist long after convalescence. In some there are finally developed a true circular insanity, manic depressive psychoses, while in others, fortunately not often, *obstinate depression,* from which after long periods most patients recover (65 per cent). The length of time during which these postpyrexial psychoses persist in favorable cases varies. It is impossible to set a time limit. My cases have averaged between 6 and 9 months. An occasional case ends in permanent insanity; here family history is of paramount importance. When *hysteria* develops after typhoid it is not to be regarded seriously—prompt treatment leads to satisfactory results. This is also true of all types of *neurasthenia.* I have seen several cases followed by *multiple cerebrospinal sclerosis,* in which the disease was progressive, following its typical course.

Posttyphoid myelitis offers nothing favorable.

Acute ascending paralysis, when complicating typhoid, will, as a rule, promptly lead to death because of respiratory involvement.

Reflexes.—Curschmann reports the behavior of the reflexes as follows: In severe typhoids, where the patients are much reduced, usually toward the end of the febrile period or during convalescence, there is decided increase of the patella tendon reflex, and marked ankle clonus. In cases of moderate severity the patella tendon reflex may be absent, normal, or oftener, feeble. Toward the end of the disease and during convalescence in these cases, he found moderate increase of the reflex. In *children* the reflex was more often absent or materially reduced.

2. Peripheral Nervous System.—Multiple neuritis and peripheral paralyses occasionally complicate typhoid fever. There are inflammatory changes in single nerves which may leave lasting symptoms—optic neuritis, auditory neuritis, and the so-called cerebral monoplegia, which is probably peripheral neuritis.

The prognosis of most peripheral neuritides is good; multiple neuritis leads to a protracted period of symptoms but, as a rule, to fair use of all of the extremities.

The so-called *typhoid spine,* painful during long periods, as a rule leads

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to a gradual full recovery, as does also *typhoid spondylitis and perispondylitis.*

The Muscular System

The *muscular system* offers, aside from its enormous atrophy, nothing of prognostic value; time returns the skeletal muscles to their normal conditions. Grave atrophic and hypertrophic changes of organic origin are rare.

The Osseous System

The lesions referable to the osseous system are not infrequent. They belong to the domain of surgery and as a rule, under proper treatment there is full recovery, even when many bones are involved in necrosis or caries.

The Ear

Complications referable to the auditory apparatus are frequent. Bezold found these in 4 per cent of typhoids. They include changes in the *external ear, such as gangrene, superficial skin lesions, decubitus, periostitis and furunculosis,* none of which are of themselves threatening. The affections of the *inner ear* may be *functional* or *organic.* But few cases of typhoid fever at the height of the disease retain normal hearing; it is most blunted with the more serious cerebral complications, when it is a part of the general toxemia. Most cases in which the changed hearing is due to functional disturbance, offer a good prognosis.

Otitis media, when uncomplicated, is promptly relieved by puncture of the drum membrane, and as a rule makes an uninterrupted recovery. Neglected cases, those associated with *deep infection* and *brain symptoms, periostitis, mastoid invasion, sinus thrombosis, and caries* are often serious, though the more serious complications of otitis media suppurativa are not as frequent with typhoid as with scarlet fever, diphtheria and pyemic infections. For the good of all typhoid patients it is always wise to examine the ears from time to time, that pus accumulations or otitis media may be promptly detected. This should be done by an expert: it may in occasional cases prevent serious complications, among these pyogenic meningitis. *Labyrinthine disturbances are rare.* When they persist they may lead to Meniere's complex with defective hearing.

Eye Complications

There are but few cases in which eye symptoms or complications during the active period of the disease, cause anxiety or influence the course of the disease; these complications are less frequent than with other serious

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infections. The *paralysis of the abducens or motor oculi, or optic neuritis, amaurosis,* are late manifestations which belong in the field of ophthalmology, and are not connected with the serious manifestations considered in the prognosis of the typhoid process itself. For their consideration and significance, it is always safest to consult the eye specialist.

Relapse

My experience with relapses—and these are veritable fresh infections—has been almost uniformly favorable. It is a rule that relapses are not so severe as the original infection. It is rare to lose a patient during an uncomplicated relapse, and these are less liable to complications than are initial infections. In my own experience I have found relapses in 8 per cent of all cases.

Typhoid Without Intestinal Lesions

The prognosis of those cases of typhoid without intestinal lesions which we meet occasionally, to which Eberth, Flexner, and Horton-Smith have called attention should be as cautiously made as that of typical typhoid. In the former we are dealing with a typhobacteremia, and it need not surprise the clinician to find some of these with profound septic symptoms, for they are due to *mixed infection.* Some were found with streptococcus, others with pneumococcus, and Lenhartz has reported a case of typhoid with staphylococcus aureus infection. All of these types make prognosis grave in accordance with the *associated toxemia* as expressed by heart, brain, lung and kidney symptoms.

Causes of Death

A thorough consideration of available and reliable post mortem findings proves that in 17.7 per cent of typhoid autopsies no complications were found, and death was due to toxemia. If we add to these the number of deaths (6.2 per cent) in which post mortem search showed but insignificant complications, the patients dying either in the first, second or third weeks of the disease, we find therefore 24 per cent (17.7 per cent and 6.2 per cent) in which typhoid toxemia may be considered to be the cause of death. Strümpell's statement is therefore justified: "In only a relatively small proportion of cases have I found death due to general infection in typhoid fever. The majority (76 per cent) of deaths are due to complications uninfluenced by treatment, and not dependent directly upon the constitutional infection."

Complications which were the causes of death in 5 per cent and over of the autopsied cases (Hölscher) may be classified as follows:

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Pulmonary edema	15 per cent
Myocardial degeneration (fatty and parenchymatous)	13 " "
Parenchymatous and fatty degeneration of the liver	10 " "
Bronchitis	10 " "
Lobular pneumonia	8 " "
Croupous pneumonia	7 " "
Pulmonary infarct	6 " "
Intestinal perforation with peritonitis	6 " "
Intestinal hemorrhage	5 " "
Edema of the brain	5 " "
Decubitus	5 " "

The changes associated with typhoid fever are far-reaching and may invade any organ of the body. A study of the preceding pages will show that the alimentary tract from the tongue to the rectum, the parotid, pancreas, liver, mesenteric glands, veins, arteries, heart, respiratory organs, the blood, the muscular system, the central and peripheral nervous systems, the skin, and the connective and bone tissue may be the seat of pathologic change; in truth, no organ of the body is immune and many may be involved at the same time. For all of these reasons it may be positively asserted that in no disease should the prognosis be more guardedly given and all that the individual case presents be more cautiously weighed.

Deaths from the Sequelae of Typhoid Fever

From the reports of the visiting nurse service of the Metropolitan Life Insurance Company as reported by Dublin, in a study of 1,936 cases of typhoid fever recorded in 1911, the following interesting features were established.

The number of cases above mentioned include 362 which were finally eliminated from consideration because the diagnosis was not considered to be accurately established. The remaining 1,574 cases make clear the effect of typhoid fever on vitality during the first three years following recovery.

It was found that 146 died while under treatment—a death rate of 9.28 per hundred. The principal complications in fatal cases were intestinal perforation, hemorrhage, meningitis, pneumonia and heart involvement.

"To determine the effect of the disease on vitality for the three years following the attack, it was necessary to compare the actual mortality of the 1,428 survivors with the expected mortality among the same class of persons. This was done by distributing the 1,428 cases by sex, color and 10-year age period, and by comparing them with similar groups taken from the mortality tables of the company for the same years. In other words, the mortality was not an arbitrary measure, but gave the death

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rate which persons of the same age, sex and color among the policy holders had experienced for the same years.

"From such comparisons, it was found that in the series of 1,428 persons the expected number of deaths was 26.45, whereas, the actual number that occurred was 54, the conclusion being that during the first three years after recovery from typhoid fever, the mortality is twice the normal. This increased rate, however, was not uniform for all three years, being greatest during the first year following recovery, less during the second year, and still less the third."

Of the 54 deaths, tuberculosis caused 39 per cent, and diseases of the heart 14.8 per cent.

Dublin concludes that in the United States there are 8,000 deaths annually among those who have recovered from typhoid fever and who yield to disease because of their reduced resistance during two years following recovery.

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II. Typhus Fever

(Spotted Fever, Typhus exanthematicus, Famine Fever (of Ireland), Jail Fever, Camp Fever, Ship Fever, Brill's Disease, Mexican tabardillo)

History.—Typhus fever was first brought to America in 1812. The credit of having separated typhus from typhoid, thus making differentiation possible belongs to American Medicine, directly to Gerhardt of Philadelphia in 1836. Jenner also insisted on typhus fever as a clinical entity separate from typhoid or enteric fever.

Plotz, a young bacteriologist, has recently established the true cause of typhus fever. His investigations were made in the Pathological Laboratory of Mt. Sinai Hospital in New York City, and the results were presented to the profession in a "Preliminary Communication" on "The Etiology of Typhus fever (and Brill's Disease)" which appeared in the Journal of the American Medical Association May 16, 1914. In his original report he claims to have found the same organism in five of six cases of Brill's disease by the use of anaërobic methods. A large number of control cases were studied and the "organism was absent from each." The bacillus is pleomorphic, "from 0.9 to 1.93 microns in length, the breadth being from one-fifth to three-fifths of the length." It is Gram-positive, not acid-fast, has no capsule, "and polar bodies can be demonstrated with appropriate methods," and it grows only anaërobically.

In a private communication from Plotz (bearing date of May tenth,

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1915,) he says: "By means of an anaërobic method of blood culture, a bacillus was isolated in pure culture from seven cases of European epidemic typhus fever, or one hundred per cent of the cases studied during the febrile period. With the same method the identical organism was recovered during the febrile period of the local endemic form of the disease in eighteen of thirty-four cases, or 53 per cent, and in two additional cases taken after the crisis similar blood cultures made in one-hundred and ninety-eight control cases yielded no such organism."

"Serological studies were carried on by Doctor Peter K. Olitsky, who has demonstrated the presence of immune bodies mostly in the apyrexial period" . . . "the same immune bodies have been demonstrated in monkeys who recovered from the disease." In guinea-pigs and monkeys who were inoculated and developed the disease the organism was recovered; the greatest bacteriemia has been found to occur early in the disease, when the temperature is highest. The pure culture of the organism can produce typical typhus fever in the guinea-pig." Plotz has demonstrated that typhus blood without bacilli or but few, is non-infective for animals. "It seems that infectivity is absolutely dependent upon the presence of a sufficient number of these bacilli."

The discovery of the bacillus by Plotz and the elaboration of a vaccine promises to prove of enormous prognostic and prophylactic value, for it is reasonable to expect that with modern methods of cleanliness, the destruction of the carrier—the body louse, from man to man—and compulsory vaccination against the disease among the belligerents, the same success will follow which we have had with the typhoid vaccine in our army.

The recent consideration of the "Etiology of Typhus Fever and the Methods of its Prevention" by Anderson strengthens the conclusions given in the preceding paragraph. He insists that "the reduction of lice infestation among the population in general," "the destruction of all lice and their eggs found on the bodies, clothing, bedding and surroundings of all cases of typhus, typhus suspects and contacts" is absolutely necessary, and will eliminate the disease because the louse is unable to transfer itself to great distances."

"The history of typhus is written in those dark pages of the world's history which tell of the grievous visitation of war, famine and misery of every kind" (Hirsch)—a frequent but justified quotation.

With positive bacteriologic data, we can more easily explain the accepted conclusion that the disease reproduces itself "in the immediate surroundings of the patient sometimes before and after, as well as during, the febrile period" (Moore).

The louse is carried on the body, clothing or other fabrics, furniture, more particularly woolly substances and furs. The contagium continues its vitality for months.

With *improved sanitary conditions* in jails, in the army, on shipboard;

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with better care of the masses in large cities, in tenements; with less filth, *epidemic typhus fever, in civilized countries and sanitary communities has become exceedingly rare.* In our own country we have had no alarming epidemic to report in over half a century, and the isolated cases which are occasionally brought to us are of a milder character than those seen over fifty years ago. In 1881 there was a small epidemic in New York of which a large number ($\frac{1}{8}$) were incorrectly diagnosed. *There was a time when one-half of all physicians in Ireland attending cases of typhus, fell victims to the disease.* In an epidemic about the middle of the nineteenth century, six of thirty-two (6 of 32) physicians at Bellevue Hospital in New York died of the disease. *The number of physicians attacked during epidemics is larger than with any other single acute infection.* The *young, active, and mentally alert,* are most likely to develop typhus during times of epidemics. *One attack gives complete immunity. Typhus fever must always be considered a serious disease.* The mortality ranges between 15 *and* 20 *per cent* in times of epidemics. Not so however in milder cases of *so-called Brill's disease,* which, if search is made and care in diagnosis is practiced, will be found to be comparatively frequent.* In 500 uncomplicated cases ending in recovery, the average duration was 13.43 days; of 100 fatal cases, 14.6 days. Patients who live beyond the 20th day and die, yield to complications rather than to typhus itself (Murchison). *Death is likely to follow during the second week.*

Foudroyant cases, beginning with fiery symptoms, so-called "sthenic fever" with full tense pulse which soon weakens, high fever, flushed *mahogany-colored face,* delirium, coma, Kernig symptom, great restlessness, opisthotonos, mottled skin, hemorrhagic eruption, involuntary stools, (though some patients may often be constipated), suppressed or materially reduced urine with evidences of nephritis or febrile albuminuria, are fatal usually during the first week.

The Pulse.—*The prognosis in those who have been previously reduced by illness or without resistance, is bad, and is the same in the aged.* The *pulse* offers valuable data for prognosis. With persistent rapidity and high fever, intermission or irregularity, pulsus alternans, with or without hurried respiration, the outlook is grave. When respiration is hurried, either due to myocardial weakness, secondary pulmonary engorgement, disseminated bronchitis or pneumonia—catarrhal or lobar—the prognosis is correspondingly worse. *Persistently slow pulse* during limited periods after the fever has subsided is not unfavorable.

The Blood.—The blood in unfavorable cases promptly shows a marked *reduction of red blood corpuscles* with a corresponding *reduction of hemoglobin.*

Average cases of typhus show moderate *leukocytosis*—12,000 to 15,000

*See last section of this article.

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though variations have been reported ranging between 1,600 to 17,600 (Krause). *The low counts, i. e., marked leukopenia are unfavorable.* Port in three cases on the third day found *leukocytic counts* of 7,900, 8,100, 14,700, respectively. He found an increase of small lymphocytes, neutrophilic polymorphonuclears 60 per cent, small lymphocytes 30 per cent, large lymphocytes 3-7.5 per cent, eosinophils 1 per cent and mast-cells not above 0.5 per cent. According to Goldberg and Anderson satisfactory evidence has not yet been adduced that the blood of the monkeys infected with typhus is virulent in the prefebrile stage and, second, it is positive that the blood of the monkey may still be virulent 24 to 36 hours after the return of the temperature to normal.

In favorable cases improvement should be apparent about the middle of the second week.

The Urine.—Diazo-reaction is present in over 50 per cent of typhus urines and is of no prognostic value. *Nephritis*—parenchymatous, particularly when hemorrhagic—adds a serious complication.

Alcoholics, early fall into a "typhoid condition" with deep invasion of the brain, marked evidences of such complication in delirium and lung invasion, when death is the usual result.

Symptoms.—The gravest cases are those with symptoms of meningitis, "coma vigil" of Jenner, pin point pupils, hemorrhagic eruption, suppression of urine with albumin and casts in the urine voided, myocardial weakness with feeble embryonic sounds, and pulmonary inflammation or congestion and meteorism.

Persistent vomiting with hiccough is unfavorable. Vomiting early in most cases is controllable; 80 per cent of typhus patients are sufficiently nourished and are carried safely to recovery without serious incidents.

Reduction in the size of the spleen—uniformly enlarged in typhus—is always favorable.

Almost all cases have more or less *catarrhal bronchitis,* which does not, unless it leads to further infection, reduce the patient's chances.

The addition of *bronchopneumonia, lobar pneumonia, empyema, endo- or pericarditis, hemorrhagic infarct or nephritis* (hemorrhagic), the latter, already mentioned, plunge the patient into a serious condition and naturally reduce the chances of recovery very materially.

Profuse perspiration is mentioned as an unfavorable symptom by some when it persists after the tenth to the twelfth day. *Peripheral neuritis,* a painful and occasional sequel, usually yields after a long period. *Relapses do not frequently follow typhus fever.*

Brill's Disease

So-called Brill's disease is now known to be a *mild form of typhus fever.* This type of the disease *runs its course in from twelve to fourteen*

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days, and terminates by crisis; convalescence is rapid. The mortality is below 1 per cent and *it is most prevalent during the autumn months.* Anderson and Goldberger working in Mexico City have *proved the identity of Brill's disease and the typhus (tabardillo) of Mexico.* They inoculated monkeys successfully, and believe that the body louse carries the infection; indeed the *monkeys were infected through the louse.* The *relationship of Brill's disease* in New York and *typhus of Mexico was further established beyond peradventure* by the experiments of these investigators, for they succeeded with the blood of Brill's disease (three patients in New York furnishing this), in carrying the infection through eleven generations of monkeys. These results are in line with those of Plotz, Baehr and Olitsky.

The prophylactic and prognostic value of these positive conclusions is of inestimable value and is "far-reaching." *The experiments further proved that one attack produced lasting immunity. Sanitarians must recognize the fact that these milder types of typhus may lead, through carelessness and failure to recognize them, to endemics and epidemics of the disease, virulent or non-virulent.*

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III. Paratyphoid Disease

Paratyphoid fever or disease includes all organic changes which are produced by infection with paratyphoid bacilli associated with bacteremia, occasionally with sepsis. The *organic diseases* which are thus produced may include enteritis, pyelitis, endometritis, cholecystitis, and meningitis (Schottmüller).

Achard and Bensaud called attention to the presence of bacilli in the pus of joints and in the urine of a typhoid patient which presented all of the characteristics of paratyphoid bacillus B. in culture media; and named the infection *paratyphoidique.* To Schottmüller belongs the credit of demonstrating in 1900 the existence of the clinical entity *paratyphoid,* and

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of tracing its origin to bacilli which admitted of positive differentiation. *The clinician will continue anxious only until he has proved by bacteriological means the characteristics of the disease-producing bacilli, thus establishing the positive diagnosis.* The diagnosis may be strongly suspected without the more painstaking and exact methods, but it cannot be fully established.

Once the *diagnosis is made positive* a favorable prognosis may be given and full recovery expected after a period of varying symptoms with irregular temperatures and convalescence, which is long and out of proportion to the benign nature of the disease. The *mortality* is not above 1 per cent, though Lorrain Smith reports 6 deaths in 162 cases. This mortality is much above that of our cases in New York State and those reported by continental observers.

There are *two types* of paratyphoid bacilli which interest us—A and B. The latter is the cause of the disease in 80 per cent of cases. In considering the conditions which may be produced by the introduction of the B bacillus, we include those cases of meat poisoning formerly considered to be due to the Bacillus enteritidis of Gärtner, which we now know is identical with paratyphoid bacillus B.

While it is not within the province of this work to consider bacteriologic methods, I add the following that prognostic conclusions may rest on safe methods of diagnosis, and that errors in differentiation may be avoided:—

Paratyphoid bacilli are actively motile, with side movements; the size of the typhoid bacillus; not colored by Gram.

Grows as an anaerobic bacillus on all culture media.

Bouillon is diffusely turbid, with a thin scum on its surface. On gelatin the growth causes a blue white opaque deposit. The isolated colonies are coarser than the typhoid culture, button-shaped and not fissured.

On agar the deposit is thin, white, gray and translucent, with characteristic gas bubbles.

On potato a grayish brown thick deposit, much like that produced by the coli communis bacillus.

Milk is not curdled, finally becomes clear and translucent; is not fermented.

In Drigalski, Conrad media (litmus milk-sugar, sodium bicarbonate, strong bouillon nutrose, and a small quantity of crystal violet B (Hoechst) deep blue colonies are grown.

Indol formation is absent in cultures not older than 1 week.

Milk- and cane-sugar are not fermented; grape-sugar is made to ferment in the presence of colonies of paratyphoid bacilli—one of the most important diagnostic features. Typhoid bacilli do not form gas in the presence of grape-sugar; the coli group do ferment milk- and cane-sugar. Paratyphoid inoculation is highly fatal to small animals (mice, rats, etc.).

In litmus whey, B produces an alkali, and type A an acid.

Agglutination continues in much stronger dilution than do typhoid bacilli, when the latter are no longer influenced. Thus Libman reports a case in which the serum agglutinated the paratyphoid bacillus B at 1 to 50, and the typhoid

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bacillus at 1 to 250. There is a diazo-reaction in 20 to 30 per cent of cases. Bacterial investigation of the blood and stools offers the safest method of reaching correct diagnostic conclusions.

Pregnancy invites invasion of the *genito-urinary* tract in the presence of paratyphoid infection.

The disease is met oftener during the summer than winter; the epidemics arise suddenly, many infected from the same source fall ill at the same time—transmission from patient direct is rare. *Paratyphoid disease differs from typhoid in the rarity of transmission from the patient direct.*

Infections due to meat or other articles of food may present active and distressing symptoms early. The *more severe cases* are those in which there is obstinate *nausea, vomiting, hiccough and weakening diarrhea.* These cases begin to mend after a few days but recover strength slowly.

The *spleen offers* no prognostic data; is uniformly enlarged.

The *blood picture* is practically the same as in typhoid fever. There is an early leukocytosis, then the characteristic leukopenia, disappearance of eosinophils, to return as the patient improves. With far-reaching enteritis there may be persistent leukocytosis. These data are of some prognostic value.

The *skin lesions,* urticaria, scarlatinal eruption, with desquamation are not unfavorable. Hemorrhagic lesions of the skin and mucous membranes are found among some of the few cases which end fatally.

Loss of flesh is striking.

Intestinal hemorrhage occasionally complicates paratyphoid (3 to 5 per cent), and is not as significant as in enteric fever.

Albuminuria is present in most cases, is moderate, without the usual accompaniments of nephritis, though the latter has complicated some cases.

The urine is markedly reduced in serious cases in which vomiting and diarrhea are excessive; complete *anuria* during limited periods has been alarming. High specific gravity with albumin, pus corpuscles, blood, casts and epithelia have been present in some of these cases.

In unfavorable cases the *temperature* may, before death, drop to 1° to 3° below normal.

Furunculosis and distant infections, joint invasion, rarely osteitis, orchitis, otitis, liver inflammation, cholecystitis—all due to the paratyphoid bacillus—have been met.

Relapses may be expected in from 8 to 12 per cent of all cases. Most *fatal cases die early, usually between the third and fifth days,* with rapid small thready pulse, distant heart sounds, cold extremities, some cyanosis, great thirst, subnormal temperature, and respiratory paralysis.

Schottmüller calls attention to the fact that patients suffering from chronic ailments are prone to develop a chronic form of gastro-enteritis

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dependent on paratyphoid infection. Most deaths are due to the severity of the primary infection or to secondary lesions which the patients are unable to withstand because of reduced resistance.

The prognosis of the abdominal type of the disease is almost uniformly favorable, as is also the invasion of the bladder and the kidney pelvis.

Cases of *puerperal paratyphoid* which have been fatal, were of a mixed type with streptococcus infection. I have never seen a case in which the cholecystitic type of the disease has occurred—if I have, it has not been recognized.

Schottmüller has reported cases in children who died of *paratyphoid meningitis.* Complications may include many of those described in the chapter on Typhoid Fever and it is to be remembered that *paratyphoid infection may follow or be associated with other acute and chronic infections,* including pure typhoid bacteremia.

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IV. Influenza

(*Epidemic Catarrh, La Grippe, Febris epidemica*)

Influenza is a disease of protean character, panepidemic, acute, due to the Bacillus of Pfeiffer (1892) which by predilection attacks the respiratory mucous membranes, is characterized by fever, marked depression, exhaustion and weakness, and is prone to give a fresh impetus to latent diseases, particularly of tuberculous nature and circulatory disturbances, while it is often followed, particularly in those of neuropathic tendencies, by long periods of nervous symptoms. Epidemics may recur at intervals varying from a few (4 to 5) to one hundred years (100).

There is an authentic account of an epidemic in Italy in 1173 A. D. In 1510 England was visited, and in 1627 the disease was brought to Massachusetts.

The disease travels as fast as travel itself, not faster. The last panepidemic which visited Europe and America was in 1889-90 when we were introduced to a disease unknown clinically to the profession of both continents. The students of medical history had only a vague conception of influenza, but to none was its clinical history clear, nor were its after effects appreciated until the profession had been taught in the school of experience.

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The disease is contagious and its *period of incubation* surprisingly short (2 to 4 days). The *mortality* of influenza does not exceed 1 per cent, including complications. The average mortality, including those given by continental and American clinicians, is 8 per cent. But few are immune to the disease though nurslings seem to escape, and the aged are attacked in smaller numbers than are the young and active. When the aged were attacked, the mortality usually due to complications, was higher than during early life. Thus in Prussia, statistics show the number of deaths and ages during years of limited epidemics as follows:—

1904	3,796	cases
1905	6,380	"
1906	2,516	"
1907	5,516	"

Of these deaths 2,004 were over 70 years of age

4,109	between	60	to	70	years	of age
1,190	"	30	"	60	"	" "
206	"	15	"	30	"	" "

The *bacteriology of influenza* is fully established. The *Bacillus of Pfeiffer* is very small, one-third the size of the tubercle bacillus, is dumb-bell shaped, usually single, occasionally in chains by end to end contact; it takes anilin dyes (carbofuchsin), is decolored by Gram, the ends stain more than the shaft; it is non-motile; is abundant in the sputum; is the cause of influenza pneumonia, and is often found with other bacteria, mainly pneumococci and streptococci.

The leading types of Influenza are:

1. Catarrhal (Respiratory)
2. Gastro-intestinal influenza
3. Influenza of the nervous system
4. Influenzal fever

1. Catarrhal or Respiratory Influenza

This is by far the most common form of the disease during epidemics, and when uncomplicated and promptly treated yields within from 3 to 6 days, leaving the patient weak out of all proportion to the duration of the symptoms. The **bronchial** and **nasal catarrh**, which is the usual accompaniment in over 90 per cent of all cases, disappears without leaving physical signs or permanent damage. In this as in all types of influenza the **enlarged spleen**, which is as a rule easily outlined by percussion is of no prognostic value.

Moderate albuminuria at the height of the disease is not uncommon without ultimate serious complication, and is not of serious moment.

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Albuminuria in catarrhal cases complicated by *pneumonia*, with evidences of *nephritis* is not to be ignored or lightly regarded. I have found *abortion rare in pregnant women* during influenza.

The complications most to be feared in the catarrhal type of influenza are referable to the respiratory organs, more particularly the lung (*pneumonia*), pleura (*pleurisy, etc.*) and also the *heart*. Mixed infection is the leading cause of secondary involvement of vital organs in catarrhal influenza, though a large number of pneumonias are due to direct infection with the Pfeiffer bacillus. *In no disease does a good prognosis depend more upon rest than in catarrhal influenza, hence the necessity for coöperation of the patient with the physician. Serious complications are thereby reduced to a minimum and the persistent anomalies referable to the heart are almost uniformly prevented even in the presence of previous weakness.*

Pneumonia most dreaded of all complications during times of influenza epidemics behaves peculiarly, and is often atypical.

During a supposed period of convalescence I have found large areas of lung tissue consolidated with all of the physical signs of such a lesion, without marked change in respiration, with slight or no fever, pulse of fair quality, not above 110, and without cough or expectoration. These cases with rest and treatment make a slow but satisfactory recovery; in the aged this complication may be the cause of sudden death.

The most serious cases of INFLUENZA PNEUMONIA in the United States during the larger epidemic of 1889-90 were those which developed early—due to the Pfeiffer infection—or developed before the end of the first week. In active subjects this was of the *lobar*—in the old, in the young and in the feeble, of the lobular variety—while in occasional cases there was a MIXED FORM in which both lungs were involved in good sized lobar deposit and islands of broncho-pneumonia.

A serious type of pneumonia complicating influenza is the MIGRATORY TYPE dependent on *mixed* (pneumococcus) or on streptococcus infection alone. These cases may lead the clinician to feel secure because of repeated *pseudocrises*, when promptly there are evidences of fresh invasion and the disease drags a weary course through several weeks; the majority of such cases die of *myocardial degeneration with more or less meningeal symptoms.*

The PURE INFLUENZA PNEUMONIA is usually catarrhal (bronchopneumonia) and offers a good prognosis in children, a fair prognosis during early life (10 to 20 per cent mortality), a better prognosis during the active years of life (6 to 10 per cent in cases treated early), in the aged a very doubtful prognosis (20 to 50 per cent, varying in different epidemics and under varying conditions of health, resistance, etc.). With all pneumonic complications *alcoholics* are seriously handicapped.

PNEUMONIA WITH INFLUENZAL MENINGITIS.—If pneumonia is added to influenzal meningitis, the prognosis is exceedingly grave. In these cases

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as in the simple influenza pneumonia, the type is bronchial, in some cases lobar, in others we find the mixed type. In some epidemics the *mortality* from this combination has been as high as 50 per cent; in others lower, as low as 20 per cent. When meningitis is purulent with pneumonia, a high mortality must be expected (over 80 per cent). Pisek reported his mortality as 92 per cent. *The majority of all deaths traceable to influenza are due to pneumonia of the catarrhal type* (Bronchopneumonia). 118 autopsies made by Hirschfeld on cases of influenza include:

11 cases of croupous pneumonia
8 " " mixed (croupons and lobular pneumonia)
24 " " catarrhal (lobular) pneumonia

Persistent cough, non-tuberculous, continues long after the acute symptoms in a few cases. These are probably due to a **chronic bronchitis** or *peribronchial change*, at times to *enlarged bronchial glands* (nodes), the latter in children oftener than in the adult, a **chronic tracheitis**, and should always demand thorough differentiation, for in some **tuberculosis** is finally unearthed. These cases continue during relatively long periods to give negative reactions and physical signs. The majority of these coughs finally yield, and the patient recovers fully.

No acute epidemic disease lights so many latent processes into activity as does catarrhal influenza; among the most frequent of these is **pulmonary tuberculosis**; usually of infiltrating character, though acute miliary deposits are not infrequent. The latter run the usual rapid course. This was particularly true of the panepidemic of 1889-90 in the central counties of New York State (For further data, see section on Pulmonary Tuberculosis).

Simple uncomplicated pleurisy, not a frequent accompaniment, offers a good prognosis, as do those cases of **empyema** which follow pneumonia. The early empyemata do not offer such a favorable prognosis, for they are only a part of acute and serious lung infection (pneumonia).

When **gangrene of the lung** follows pneumonia, the majority die with symptoms of sepsis and exhaustion.

Abscess of the lung if detected and relieved by operation, offers a fair chance of recovery.

Bronchiectasis may result from one or both of the two preceding complications; if the patients live, the condition continues to be chronic, more or less troublesome according to the size and location of the bronchial dilatation.

Pulse and Heart Changes.—With all the complications of catarrhal influenza the pulse offers the usual prognostic data as in other acute infections.

Persistent changes in the pulse and heart which are often more alarm-

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ing to the patient than to the physician, are likely to be late, and may follow any of the types of influenza. The number of *cardiac anomalies and arhythmias* following the infection is very large; they are dependent on either myocardial weakness or functional disturbances of the heart.

Intermittence is present as a rule in these cases; occasionally *tachycardia* alternates with *bradycardia* or the latter is a postfebrile or postpneumonic sequel; in all there is an enormous element of neurasthenia. Fear takes possession of the patient. In the larger proportion of cases the heart finally, after a long period, falls into better habits, and returns to normal. *Early dicrotism* need not be considered of serious nature.

In rare cases, probably where the heart muscle was already the seat of some disease, *fatty degeneration of the heart muscle with thrombosis* in both ventricles has been found post mortem and occasionally GANGRENE of the lower extremities has developed in these cases (Eichhorst, Gerhardt).

Relative mitral insufficiency is an expression of heart weakness which yields to rest in most cases with the disappearance of the systolic murmur.

An occasional case develops fatal MALIGNANT ENDOCARDITIS or the less serious type of the disease or, rarely PERICARDITIS.

Ear Complications.—With catarrhal influenza ear complications often retard recovery. OTITIS MEDIA, either suppurative or non-suppurative, SINUS DISTURBANCES, MASTOIDITIS, all postpone convalescence or are early complications, *all* of which *offer good prognoses if promptly treated.* In only occasional cases which have been under treatment during reasonable periods, has meningitis developed from aural infections.

Serious **hemorrhagic diathesis** with influenza, types of complicating purpura, have added depressing factors in occasional cases (Pick). In America we have seen but few of these.

Other complications include disturbances of one or many organs in individual cases; many will be mentioned in connection with other forms of influenza in the following pages; the prognostic significance of all of these cannot be separately considered but will receive attention in connection with the diseases of the separate organs.

2. *Gastro-intestinal Influenza*

As a rule the gastro-intestinal form runs a short course, during which the patient is uncomfortable for from 2 to 5 days because of the *vomiting,* at times *obstinate watery diarrhea, abdominal pains, tender peritoneum* and *rarely ulceration* in either the small or large intestines.

In most of these cases there is *enlargement of the spleen.* The latter is proportionate to the severity of the infection.

The *prognosis* of gastro-intestinal grip is good, though full recovery (return to normal resistance) is slow. Heart and other complications are not infrequent, the lungs are but rarely involved.

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3. *Influenza of the Nervous System*

The nervous system may be either (a) *primarily* or (b) *secondarily* involved by the Pfeiffer infection without catarrhal symptoms.

(a) **Primary invasion** of the nervous system, leads to a train of positive symptoms, varying according to the severity of the disease.

In CHILDREN there may, even in favorable cases be *convulsions,* early evidences of *meningitis, the presence of the infecting agent in the withdrawn lumbar fluid,* or there may be *active delirium* during a limited period. Most of these cases terminate favorably. In the ADULT the primary symptoms are less severe as a rule, and the *outlook from the beginning is favorable,* in spite of great prostration, severe headache, annoying myalgias; in the severer cases there is delirium and at times somnolence; occasionally insomnia.

PRIMARY PERIPHERAL LIMITED NEURITIS, leading to severe NEURALGIA is favorably influenced by treatment.

(b) **The complications due to organic change** in the nervous system at the height of the disease or manifested early, are of serious nature.

With alcoholics "WET BRAIN," ALCOHOLIC MENINGITIS with all of the symptoms of DELIRIUM TREMENS may lead to death in DEEP COMA from the sixth to the tenth day.

ACUTE ENCEPHALITIS simulating CEREBRAL APOPLEXY, with or without *motor paralysis* or *aphasia,* occasionally MONOPLEGIA—usually of an arm —may promptly cause death.

MENINGITIS with MASTOIDITIS, VENOUS THROMBOSIS, or SECONDARY MENINGITIS TO CATARRHAL INFECTION OF THE NASOPHARYNX is serious unless the condition is promptly recognized and surgical relief is obtained.

SECONDARY MULTIPLE NEURITIS offers a good prognosis; recovery is slow but restoration of function is likely to be complete.

ABSCESS OF THE BRAIN is not frequent; it has occasionally been found post mortem. My records offer no well authenticated case diagnosticated ante mortem save those secondary to otitis media and mastoid invasion. The *prognosis* in reported cases has been very bad.

The *statistics* of our state hospitals for the care of the insane gathered after the panepidemic of 1889-90, prove the enormous influence of influenzal infection in causing PSYCHOSES. Our hospitals were filled with all varieties of psychoses usually developed during convalescence. In some there were long periods of depression (melancholia), in others exhilaration and hallucinations. Those not seriously burdened by heredity ultimately returned to full health.

NEURASTHENIA in all of its forms may develop; it yields slowly after months of patient waiting or the fully developed habit may persist, to make the victim wretched during years or forever.

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Myelitis and occasional ascending paralysis (Landry's type) have been noted and are mentioned by Romberg and Osler.

A study of the literature of these complications does not justify an encouraging forecast; no one man has a large material at his command, for the association of the myelitis of Landry's syndrome with influenza has been limited.

4. *Influenzal Fever*

Occasional cases without the usual catarrhal symptoms present with marked features; there is *irregular* fever, at times it is *continuous* and the patient falls into a *typhoid condition;* the fever may be *remittent,* with or without chills; there are no lung complications as a rule.

These febrile types may present a variety of pictures, but the *prognosis* in the uncomplicated cases is good, though there may be great *prostration,* at times *cardiac anomalies* and *psychoses* long after the disappearance of acute symptoms. Any of the complications associated with the other forms of influenza may develop in exceptional cases. The respiratory organs rarely suffer.

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V. Pyogenic Infections—Septicemia—Pyemia

(*Sepsis, Blood Poisoning, Septicopyemia*)

Septicemia is a general disturbance due to the presence in the blood of septic, disease-producing bacteria or their products, i. e., toxins. Septicemia may also be defined as a *bacteremia* or *toxinemia* (*sapremia* when products of decomposition are included). It is possible for *sepsis* to include the presence in the blood of both bacteria (bacteremia) *and toxins* (*toxinemia*) at the same time. In contradistinction to pyemia (a surgical affection), sepsis does not include suppurating metastatic foci. In all cases of sepsis, toxins finally become the cause of the general, i. e., constitutional symptoms, and are responsible for the consecutive degenerative changes in the vital organs of the body, i. e., heart, spleen, kidney, etc.

Grave constitutional disturbances with degenerative changes may lead to death without evident bacteremia, as proved by blood cultural methods; these effects are always due to the overpowering toxinemia.

Most constitutional infections are secondary to a primary local focus

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through which, or from which bacteremia and toxinemia proceed (puerperal sepsis, anthrax, pneumonia, gonorrhea, etc.). There are, on the other hand, *grave forms of sepsis* in which the constitutional disturbances are due to a prompt dissemination of disease-producing germs (streptococci usually) without known or evident local lesion from the blood stream to the vital organs, with the associated baneful and malignant results of toxic poisoning. These are the cases which offer the gravest forecast. There is always *danger of septic deposits in organs which present changed or diseased surfaces to the blood and lymph stream. This is manifest in one of* the gravest forms of septicemia—*malignant endocarditis.* In these cases, there is often grafted upon an *old endocardial or valvular lesion* an acute septic and malignant endocarditis from which, by the detaching of vegetations to distant parts (emboli), grave complications (hemorrhagic infarcts) are added, which presage an absolutely unfavorable outcome. The *septic type of endocarditis* will be separately considered in connection with the diseases of the heart (See Septic Endocarditis).

The search of the invading bacteria for a port of exit (elimination) leads to serious kidney change, i. e., *septic nephritis* in the graver forms of blood-poisoning, with the characteristic urinary evidences, which is never to be lightly regarded. Marked reduction in the quantity of the urine secreted, lowered urea output, albuminuria, large numbers of casts with evidences of invasion of the nervous system, are among the *symptoms* which call for a guarded, usually a bad prognosis.

The *staphylococcus infections* offer a more favorable prognosis than do the streptococcus. The latter infections, though grave do not always lead to death. (The staphylococcus does not enter the blood-stream so easily or readily as does the streptococcus, but when it does it has recently been held by pathologists that it is much more serious. This question is still *sub judice.*)

The *streptococcus* is less likely to cause pyogenic processes (abscesses) than the staphylococcus. It enters the blood stream quicker and with greater ease than does the staphylococcus. Once the staphylococcus has caused bacteremia, it is a question whether it does not offer a less favorable prognosis than does streptococcemia.

Many *forms of septic and pyemic infections* are likely to be *mixed,* complicating many other primary infections to which reference has been made in other chapters; these include, **diphtheria, pneumonia, tuberculosis, typhoid fever,** etc. Such mixed infection, as has been repeatedly demonstrated, adds a large element of danger.

Organic diseases of the vital organs invite infections which are largely responsible for the death of the individual. These are considered *"terminal infections."* Osler quotes Flexner, who analyzed 255 cases of chronic renal and cardiac disease in which full bacteriologic examinations were made at the autopsies "in which 213 gave positive, and 42 negative results."

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The infections were local and general; the former were common "in a large proportion of all cases of Bright's disease, arteriosclerosis, heart disease, cirrhosis of the liver, and other chronic disorders." In these cases it was found that acute pleurisy, pericarditis, peritonitis, meningitis or endocarditis were the usual seats of local infection.

The *most serious infection* associated with previously existing organic disease is the *streptococcus.*

General gonococcus infection, when associated with **gonococcus endocarditis**—and it is very often—has in my experience been uniformly fatal. Flexner contends that "the blood serum of persons suffering from advanced chronic disease was found by him to be less destructive to the staphylococcus aureus than normal human serum." Lenhartz's statistics show that 75 per cent of all general sepsis is dependent upon *streptococcus infection. Staphylococcus and pneumococcus infections* are responsible for 8 to 9 per cent.

The *female generative tract* is the most frequent source of general infection, due to unclean hands, instruments, clothing, usually to preventable factors for which the physician is not always responsible. Surgical operations with consecutive infections are also a fruitful source of septic poisonings.

Phlebitis with or without septic thrombosis must always be considered a menace, and when due to streptococcus infection is a serious complication. **Septic thrombosis,** with single or multiple thrombi, is a serious complication with any form of sepsis; the prognosis is grave, depending largely on the *depth of the toxinemia,* the *pathologic changes in vital organs* (heart and kidney mainly) and the *location of the thrombus.*

Apparently innocent local infections without grave initial symptoms may lead to grave constitutional disturbances due to bacteremia and toxinemia, or to changes in vital organs, with pus-producing organisms (pyemia), to multiple abscesses in the various organs of the body. Thus simple *follicular* (streptococcus) *tonsillitis* offers innumerable examples of the truth of this possibility. *Other examples* are otitis media, bone invasion, suppurating hemorrhoids, superficial or deep skin infections, prostatitis, urethral abscess, gonorrhea and trivial injuries. The *prognosis* is always clouded when there are *multiple abscesses associated with pyemia* in the *lung or liver,* or in both at the same time.

The *height and behavior of the temperature* serves as a valuable guide in connection *with the pulse* for prognosis.

With pyemia, multiple abscesses, purulent phlebitis and thrombosis, the character of the *fever* is likely to be *intermittent,* and profuse sweats follow with a fall of temperature. *Severe chills* in these cases are the rule.

When with pus-producing infections there are *long periods of apyrexia between the chills,* the prognosis is more favorable than in cases with continuous elevation of temperature—barring, however, those cases of *malig-*

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nant endocarditis of the intermittent type, which always offer a grave forecast.

Chronic cases due to the streptococcus viridans may remain afebrile during several days, or the temperature may be but slightly elevated with or without the chronic form of endocarditis, for which this strain is responsible; the prognosis remains bad and the attendant is not to be deluded by the apparent improvement.

Cases in which the *temperature gradually falls to normal or below,* with improvement of pulse and other constitutional symptoms offer a good prognosis, but in these, it requires more than a few days of the afebrile state before a positive opinion as to the outcome is justified.

The effect of the toxinemia on the vasomotor system through the spinal centers is of paramount importance. If the heart, though rapid, shows no evidences of insufficiency, its separate sounds remain clear and fairly strong, and endocarditis does not develop, there is at least a powerful staff upon which we may continue to lean.

Dilatation of the heart with relative mitral insufficiency, with or without accentuation of the second pulmonic sound and rapid pulse, persistence of fever, nephritis, and evidences of cerebral invasion, offer a bad prognosis.

Patients developing *sepsis* from whatever source, with *pre-existing endocarditis* are handicapped, and in these the prognosis is always doubtful.

The *influence of hemorrhagic infarcts* is always bad; to these we again refer in the chapter on Malignant Endocarditis.

The *blood* shows *marked leukocytosis* in most cases of sepsis with reduction in the number of red blood corpuscles. There are cases of fully developed sepsis in which the blood picture is not materially changed. Limbeck has reported cases of puerperal sepsis without leukocytosis. *The blood offers no data so far as the count or appearance of its corpuscular elements are concerned which influence prognosis.*

The *degree of bacteremia* in occasional cases does influence prognosis —favorable in accordance with the number of bacteria in the blood stream.

Pneumonia as a complication of sepsis or pyemia is always serious. *Frequent respirations* are not always due to pneumonic consolidation, but to a number of factors including heart weakness, muscular enfeeblement, hemorrhagic infarct, etc.

The **spleen** is always more or less enlarged with all forms of blood-poisoning. It offers no prognostic data.

The grave forms of sepsis are complicated with cerebral and meningeal symptoms.

Septic meningitis is usually a fatal complication; with **erysipelatous inflammation,** it always proves serious (See Erysipelas).

Duration.—The duration of all forms of blood-poisoning depends upon the source and extent of the primary lesion, the life history of the infecting germ, and many other factors. *Acute sepsis* may kill in a few days.

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Atypical cases, particularly streptococcus viridans infection with endocarditis, runs a chronic course covering many months. We recently saw a case which died at the end of the fourteenth month, of cerebral infarct. The *average duration* of septic processes may be safely placed between 5 to 8 weeks. Pyemia is often chronic. *Sudden death* in acute or chronic cases may be due to thrombosis or embolism, cardiac insufficiency, pneumonia or a variety of complications considered in connection with the special diseases. Pneumococcemia is separately considered.

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VI. Diphtheria

General Considerations

Bacteriology.—Diphtheria is an acute infectious disease, due to the Klebs-Loeffler Bacillus (1883-1884) (a short rod-shaped microörganism, which may be curved or club-shaped at one end. Gram-positive, it shows polar granules when stained with methylene-blue, with characteristic arrangement in groups like Chinese figures) contagious, attacking by predilection the tonsils, uvula, soft palate, postnasal space and larynx, extending into the trachea and bronchi and invading the lung in the graver infections, with evidences of general toxemia. The disease is *sporadic* and *epidemic. Uncontrolled, the infection is always serious and associated with a high death rate, but is favorably influenced by the Behring antitoxin (1892) in almost all cases, if treated on the first day.*

History.—The disease is now prevalent in all parts of the civilized world, attacks the young especially, rarely the aged, though it is not infrequent in adults during middle life. In 70,000 cases collected (London Lancet, 1878) the cases were distributed as follows, according to ages:

Under 12 months	9	per cent
1 to 5 years	45	" "
5 to 10 "	26	" "
10 to 15 "	9	" "
15 to 25 "	5	" "
25 to 45 "	3.5	" "
45 years and over	2.5	" "

Jacobi's case is the youngest on record and was 9 days old. The statistics of the New York Health Department (1891-1900) show that 80.8

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per cent of deaths occurred under 5, and 17 per cent between 5 and 10 years. The disease was known before the Christian Era (angina maligna, angina gangrænosa); in Spain, where there were epidemics at short intervals between 1553 and 1618; in Italy, from 1610 to 1650; in France as early as 1736; 1744 in England; 1752 in Germany, and the same year it appeared in America.

Bretonneau's description of the disease remains among the classics of medicine, as well as that of Trousseau (1821-1828). There can be no doubt of the fact which clinical experience and a study of medical literature prove, that the *character of the disease*, its *virulence* and *mortality*, are influenced by unknown factors, and vary materially with fresh epidemics and during different years. The various *seasons* of the year do not influence the mortality of diphtheria, though the disease is more frequent during the winter months.

In Germany the mortality reached its climax in 1886 with 122,000 deaths. In 1900 there were 45,000 deaths. In 1885 the number of deaths due to the disease in Germany was 122.7 per 100,000; in 1895, 54; and in 1905 only 22.4. Nuttall and Smith offer the following figures, showing the maximum and minimum death rate due to diphtheria in 100,000 of inhabitants in Boston, Providence, New York and St. Louis:

	Maximum.	Minimum.	Period of Observation.
Boston	163 in 1881	51 in 1891	1861–1895
Providence	314 in 1877	8 in 1868	1868–1895
New York	208 in 1877	23 in 1873	1868–1893
St. Louis	314 in 1877	8 in 1868	1868–1895

Factors Influencing Growth of Disease.—The body, including the blood and mucous membrane particularly, offers marked resistance to the disease. There are factors, as Trumpf has demonstrated, which are necessary for the development of the disease.

They are:

1. A *high degree of virulence* of the infecting agent.
2. The *deposit of large numbers of bacilli* on the mucous membrane.
3. The *membrane must be in a suitable condition* to offer a habitat for the proliferation of the bacillus.
4. The infected individual must be *susceptible;* hence this factor and the others are variable, protect or expose the same subject to the disease at different times.

Mixed infection with pneumococci, staphylo- and streptococci, influences the prognosis of diphtheria materially.

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A degree of *immunity* is developed by a single diphtheria infection. *Diphtheria infection* added to already existing *scarlet fever* is not associated with the same danger as is the addition of scarlet fever to diphtheria (Uppenheimer).

Zucker's statistics show second attacks in only 0.9 per cent, and third attacks in 0.13 per cent of cases.

Carriers.—Malignant as well as *benign diphtheria* may be conveyed by "carriers" who may or may not have had the disease. The *mildest type* of the disease in one individual may transmit the most malignant form to others.

Pharyngeal Diphtheria

The following is the classification of pharyngeal diphtheria, under which the subject will be treated:

1. Mild infection of the fauces, tonsils, without severe general toxemia.
2. Pharygeal infection with severe general toxemia.
(a) Non-gangrenous
(b) Gangrenous

I. Mild Infection Without Several General Toxemia.—With mild infection of the tonsils and surrounding tissues, there are generally no evidences of severe constitutional toxemia, and if the case is recognized on the first or during the second day of the disease and promptly injected with a sufficient number of antitoxin units, improvement is prompt as a rule, the *membrane begins* to disappear, *fever and pulse* improve, *glandular enlargements* recede, and between the sixth and tenth day *convalescence* has commenced and in the majority of cases is uninterrupted. Cases which begin with *laryngeal invasion* so limited as to cause but few symptoms, with *croupy cough,* but without other evidences of laryngeal stenosis, may later "ascend" with invasion of tonsils and but few constitutional symptoms, when the *prognosis* is less favorable than in the first mentioned cases—because time has been lost before active treatment was commenced.

If *laryngeal diphtheria* in these cases does progress in spite of the failure to make an accurate bacteriological diagnosis early, the *prompt treatment* of the disease after the appearance of pharyngeal diphtheria will lead to recovery in over 85 per cent of such cases. If from these apparently mild cases there is progression to the posterior nares, and greater invasion of the cervical glands there will, as the process advances, be evidences of increasing toxemia. Fever may not be high, but the *heart* and *kidney* may suffer most, and the prognosis is accordingly influenced unfavorably. Leukocytosis is present in all of these cases. Its influence on prognosis will also be studied in connection with the administration of antitoxin—to which reference will be made later in this chapter. The *prognostic value of leukocytosis,* has been epitomized by Kautback and Andrews as follows:

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"1. A high leukocytosis signifies a good reaction and is present in those cases which recover.

"2. A low leukocytosis at the height of the disease, before antitoxin has been injected, accompanies most, if not all fatal cases.

"3. The high leukocytosis of well reacting cases after and during antitoxin treatment steadily diminishes, the number of cells decreasing by 50 per cent in 3 or 4 days."

Cases which begin in the *nose* with descending disease, i. e., final deposition on *tonsils* and *soft palate,* even without constitutional symptoms at first, are usually complicated with painful enlargement of the lymphatics, increasing anemia, and before the fifth or sixth day there are in many cases evidences of toxemia, albuminuria, normal or subnormal or slightly elevated temperature, and with increasing heart weakness the patient's condition becomes grave. These complications with beginning *nasal diphtheria* are as a rule prevented if the disease is promptly recognized, and the patient injected. *Albuminuria* without other symptoms or microscopic elements denoting nephritis, is present at sometime in the majority of these cases, and does not cloud the prognosis.

II. Pharyngeal Infection with Severe Toxemia.

(a) NON-GANGRENOUS PHARYNGEAL DIPHTHERIA WITH SEVERE TOXEMIA.—The majority of pharyngeal infections which are associated with severe toxemia are found among the poorer classes, in tenements and homes where there are many children, where the physician is rarely called early and the process with its overpowering toxemia is far advanced before treatment is instituted. In these cases, as a rule, there is some nasal invasion also; the general appearance of the patient is unfavorable, color pale, face puffy, at times ashen; breathing rapid; pulse accelerated, small and without character; urine is reduced in quantity and albuminous, with hyaline and granular casts; temperature behaves irregularly, at times is high, in some cases subnormal or only slightly elevated, the odor foul. In these *non-gangrenous cases,* there is less sloughing of tissues, but the membrane presents a greyish brown or dirty yellow appearance; the discharge from the nares is at times watery, almost continuous, ichorous, causes ulceration of the skin; and in spite of large doses of *antitoxin* there is a large mortality, ranging between 15 and 50 per cent, depending upon the *day of injection,* the *extent and character of the associated lesions* and the *depth of toxemia.* Albuminuria with casts, when an expression of acute non-suppurative nephropathy (Councilman pathology), or glomerular or tubular invasion, adds an element of danger.

(b) GANGRENOUS PHARYNGEAL DIPHTHERIA.—The gangrenous form is always serious. These cases may arise sporadically or during epidemics; they show the character of the infection. Trousseau in 1846 called attention to these cases. They have become less frequent during the past 20 years. In gangrenous diphtheria we have the picture of deep sepsis with

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all of its classic constitutional symptoms to make the prognosis exceedingly grave. There are in the worst cases dark brown, blackish, foul-odored sloughs, with other local manifestations and swelling of glands; foul dry brown tongue; cracked ulcerated lips, almost continuous dark or bloody nasal discharge; increasing weakness; great thirst; thready pulse; albuminuria, usually some form of nephritis. In occasional cases death follows a number of hours of urinary suppression after coma or disturbed sensorium, including delirium and great unrest. In these cases there is likely to be hypoleukocytosis which is unaffected by *serum injection.* Acetonuria and acetonemia with glycosuria may be present in the gravest cases.

Gangrenous cases developing laryngeal stenosis offer most unfavorable prognoses.

Hoarseness, gradually increasing with this and most forms of diphtheria, is an ominous symptom and usually leads to stenosis, if the patient lives long enough. Cyanosis, rapid pulse, delirium, noisy respiration showing extreme stenosis, with air hunger—a pitiful picture of suffering —usually end the scene (carbonic acid poisoning).

Nasal Diphtheria and Laryngeal Diphtheria

Nasal and laryngeal invasion (*stenosis*), as has been emphasized in connection with all forms of the disease, are always of serious significance whether primary or secondary.

Skin Diphtheria

There are in some cases *diphtheritic ulcerations of the skin.* The invasion of the skin alone is rarely met without pharyngeal deposit. Its prognosis is relatively favorable when primary, depending on the degree of virulence and the time of injection.

Conjunctival Diphtheria

Conjunctival diphtheria is not often seen in hospital or private practice. Occasionally during epidemics a case arises, in which with nasopharyngeal disease the conjunctiva is infected. Unless improvement is prompt and the case has received early treatment, the danger to the eye is great and destructive ulceration may result.

Diphtheria of the Vulva

My experience includes 4 cases of vulvar diphtheria, all seen during the *puerperal period.* All had been treated for puerperal sepsis; in 3 fortunately the antitoxin and local treatment saved the patients. 1 case seen during the preantitoxin period died with all the symptoms of puerperal peritonitis.

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The amount of *glandular invasion* is as a rule proportionate to the extent of the nasopharyngeal involvement, and is an expression of the malignancy of the process in most, but not in all cases. There is but slight swelling of the glands in occasional cases of great virulence; on the other hand I have seen a goodly number of cases in which benign diphtheria was associated with glandular enlargement out of all proportion to the deposit, or to the extent of the disease.

Complications of Diphtheria

Nephritis complicates 50 per cent of all diphtherias. Councilman considers this a true non-suppurative interstitial nephropathy; in some cases there is hemorrhagic nephritis, at times atypical forms resembling parenchymatous disease of the kidney. The albumin loss is moderate, less than with scarlatinal nephritis; there is also less dropsy—often none.

ALBUMINURIA may in the milder cases prove to be transitory; the amount of albumin offers no prognostic data. In the severe and malignant types, nephritis may show but slight albuminuria in the presence of the gravest possible conditions. It may be concluded that cases which are albumin-free offer a better prognosis than do those in which it is present, from whatever cause.

If albuminuria is transitory, the prognosis is as a rule good in the absence of heart weakness or other depressing conditions.

With nephritis and scanty urine, abundant casts, (hyalin, granular and blood) the prognosis is unfavorable. UREMIA may end life within a limited period. This is not frequent.

Diphtheritic nephritis does not cause DROPSY. When the latter is present, it is due to circulatory embarrassment and is a serious complication.

CHRONIC NEPHRITIS may develop after the acute symptoms have disappeared. This may be overlooked unless the cases are followed. The prognosis will be further considered in the chapter on nephritis.

Heart Complications.—The heart is subject to *myocardial change* in all cases of diphtheria, the extent depending entirely upon the *malignancy of the toxemia;* its muscle may undergo either interstitial change (MYOCARDITIS INTERSTITIALIS), fatty, or parenchymatous degeneration.

The *interstitial type* of myocarditis is the most frequent cause of heart weakness in diphtheria (Jores, Romberg and others). The prognosis as influenced by the heart, depends on the extent of the degeneration or myocarditis. In the milder cases this is limited, in the gangrenous toxemias it is far-reaching. With dilatation, weak heart sounds, rapid small pulse, with or without murmurs, the prognosis is bad.

IRREGULARITY OF THE PULSE during the acute and toxic period of the disease is always serious; later however, during convalescence with or without paralyses, it is less serious, and great rapidity of heart action and

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erratic hearts are often well borne during long periods, leading ultimately to recovery.

Endocarditis and Pericarditis if present are due to secondary infection. They are likely to prove malignant and offer a grave prognosis (*malignant diphtheritic streptococcus endocarditis*).

Sudden Death.—There is in the profession a fixed belief that diphtheria often leads to sudden death. This is not based upon clinical observation, and is unjustified by experience.

Patients rarely die suddenly during the period of convalescence or at the height of the disease. I am in full accord with Harris, who says: "there have always been timely warnings of danger." Experience proves that the heart weakness or other cardiac anomalies offer positive symptoms and physical signs, during a period of sufficient length to make their presence recognized. Careful examination of the heart, repeated daily during convalescence, will give sufficient warning of a failing degenerated heart muscle; the same is true of all periods of the disease.

It will be necessary in adding to other prognostic signs, the data offered by the heart, to consider as Harris has suggested:

1. The heart sounds
2. The position of the cardiac impulse
3. The pulse
4. The outline of cardiac dullness.

Irregularity with reduplication of the second sound and galloping rhythm are always serious.

Relative mitral insufficiency may persist for an indefinite period; in the absence of other grave symptoms, without extreme dilatation, these patients recover and the murmur ultimately disappears.

Tachycardia due to paralysis of the pneumogastric, is often well borne by most children during long periods. To this I will again refer when considering diphtheritic paralysis.

Embolic Infarcts are rare; if present they are an expression as a rule of malignant endocarditis or septic processes, and are therefore serious complications.

Purpura, petechiæ, hemorrhages from mucous membranes are associated with heart weakness in malignant cases and are of grave import.

Diphtheritic Paralysis.—Paralysis is a complication or sequel of diphtheria in about 12 per cent of all cases, and *is by no means an expression of the severity of the diphtheritic infection.* I have seen a number of cases which were so mild that no physician had been called, which were treated by mothers for *mumps*, in which paralysis developed. Often the gravest infections are entirely without this complication.

Paralysis as a rule is a *sequel* of the disease, developing from 3 to 10 weeks after infection.

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In severe cases GLOSSOPHARYNGEAL PARALYSIS becomes a serious complication as early as the fifth to the eighth day. In these, the chances for the patient are unfavorable.

SIMPLE UNCOMPLICATED PARALYSIS OF THE SOFT PALATE when it follows the acute stage, offers a favorable prognosis; recovery may be expected in from 3 to 10 weeks.

Paralysis which interferes with deglutition, (*glossopharyngeal*) WITH CHOKING COUGH, is always more serious than paralysis of the soft palate alone. It may lead to "*Schluck pneumonia*" or *sudden asphyxia*. Paralysis associated with changes in the voice, an unsatisfactory and inefficient cough, without a normally closing glottis, is always to be feared because of the danger of pneumonia from the entrance of food etc. into the air passages. Many of these cases, under close watching and feeding, recover slowly.

PARALYSIS OF THE EXTREMITIES, usually most developed in the legs, if not associated with severe glossopharyngeal or *pneumogastric paralysis*, tends to full but slow recovery, requiring from 5 to 10 months.

I have never in my own practice seen a case of HEMIPLEGIA with diphtheria. A number have been reported; probably these were embolic, thrombotic, or due to cerebral hemorrhage. The prognosis must of necessity be grave, but recovery is not impossible. Rolleston, in 9,075 cases of diphtheria included 6 of hemiplegia, of which 4 died. In 1 of these there was an embolus in the cerebral vessels. When the respiratory muscles are involved (PNEUMOGASTRIC PARALYSIS), the prognosis will be grave in proportion to the extent of the respiratory embarrassment. In these cases there is, as a rule, associated tachycardia. While the complication will always cause the attendant great anxiety, and is serious, let him remember that in extreme cases recovery may follow. Long continued pneumogastric paralysis with fully developed symptoms have in my experience finally yielded, and full restoration to health has followed with normal pulse and respiration, in a number of cases. No positive prognosis can be given; the patient until fully restored stands on the edge of a precipice, and may fall at any moment. OCULAR PARALYSES may be the only evidence of diphtheritic palsy, or these may be a part of multiple neuritis and far-reaching paralysis. The prognosis is as a rule favorable when limited to the eye muscles. *Nasal diphtheria* is likely to be followed by paralysis of the lower extremities, at times by QUADRIPLEGIA. The prognosis, if this is a late complication, is good. *Fully developed paralysis which develops at the height of infection offers a very bad prognosis.*

Have the number of diphtheritic paralyses been increased by the use of the von Behring antitoxin? This question can be answered without qualification in the negative. There are a larger number of diphtheritic paralyses, it is true, but not because of antitoxin. There are fortunately a larger number saved, hence the increase of paralyses; our observation

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of cases is closer, a larger number are recorded by health authorities than formerly. Neither the close study of this subject by Rolleston, nor the statistics of Fibigan prove that the Behring serum has "altered the incidence to any appreciable extent."

Persistent vomiting during the acute period of infection is either due to diphtheria of the stomach, nephritis, cardiac insufficiency or other serious conditions; if unrelieved, there is cardiac incompetence, and death follows.

Pneumonia.—Pneumonia (lobular) is found in at least 50 per cent of autopsied diphtherias. When developed early it is among the complications least amenable to treatment, and death is likely to follow. The unfavorable symptoms are increasing dyspnea, cyanosis, rapid small erratic and irregular pulse, physical signs of collapsed lung, and inability to cough, with hurried respiration and evidences of toxic nephritis.

Pleurisy—serous and purulent—are not frequent; when late, less serious than early.

Otitis media suppurativa may be an early or late complication. Recovery follows unless it is present during the height of malignant infection, when it is simply one of many conditions which cloud the prognosis.

Liver and spleen offer nothing of importance for our purposes.

Parotitis is not frequent, but if present is likely to be an expression of profound toxemia and always secondary.

Relapse

Relapse occurs occasionally. In some cases the *habit of reproducing membranous deposit* is formed and is encouraged by the use of local treatment; such cases if left untreated, promptly recover as a rule.

Relapse immediately after acute infection or as the membrane is cast off, aggravates all symptoms, retards recovery, but offers a good prognosis if the patient is not exhausted and the disease is non-malignant. Associated complications (nephritis, myocarditis, etc.) naturally modify the prognosis.

Diphtheria and Antitoxin

Blood Counts after the Injection of Antitoxin.—Prognostic data may be furnished by blood-counts before and after the use of the serum.

Hypoleukocytosis follows the injection of the serum; if after 3 or 4 hours the *leukocytic count* present before injection is not reached, the prognosis is unfavorable. A return to a higher leukocytic count after injection than was primarily present is favorable. In unfavorable cases the hypoleukocytosis continues after injection; there is no effort to increase *phagocytosis* (Simon).

Serum Sickness.—Methods have been and are being devised which have

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reduced serum sickness materially. The use of calcium chlorid has been efficacious (Netter-Consin-Gervin).

Serum sickness is present where horse serum was used:

In cases where 1,500 units were injected in 8.6 per cent

In cases where 1,500 to 4,500 units were injected in 13.13 per cent

In cases where 4,500 units and upward were injected in 18.91 per cent.

While painful arthritides and eruptions have followed the use of the serum in my practice, I have never recorded a death traceable to it. The use of lamb serum (Ascoli) offers encouragement, for by it, serum sickness becomes an infrequent complication. It will however prove more difficult to obtain a sufficient supply of this than horse serum. Behring's newer methods will reduce this complication, it is hoped.

It requires no extensive argument in considering the *prognosis* of diphtheria to prove to the clinician as well as to the lay world the fact that the addition by von Behring (1892) of his *antitoxin* to our armamentarium at once added *a remedy* which *promptly changed the prognosis of the disease.*

Within 3 years after its introduction, von Behring proved that in Berlin at the Charité in cases where antitoxin was used the mortality was reduced to 8 per cent against 32.7 per cent in the Berlin Bethany Hospital, where it had not yet been introduced. These and the figures which are to follow, with the experiences easily obtained from those who practiced during the *pre-antitoxin period* and have been privileged to continue their observations since, are sufficiently convincing. We now enter the treatment of the disease with reasonable certainty of success, formerly it was with fear and a painful appreciation of the limitations of our art to combat the monster.

Baginski has demonstrated a mortality of 15.8 in 10,000 inhabitants before the use of antitoxin; since its use a reduction to 2.4 in 10,000 in 1908, and as low as 3. in 10,000 in 1907—the year of a severe epidemic in Germany.

Further, I offer the following collective statistics:

Name of Investigator.	No. of Cases.	Mortality, Per Cent.	Mortality when Serum was injected on					
			1st Day.	2nd Day.	3rd Day.	4th Day.	5th Day.	6th Day.
Welch.....	1,489	14.2	2.3	8.1	13.3	19.0	29.3	34.1
American Pediatric Society (Collective Investigations).....	5,794	12.3	4.9	7.4	8.8	20.7	35.3	....
Kaiserl. Gesundh. Amt. (Collective Invest.)....	9,581	15.5	6.6	8.3	12.9	17.	23.	....

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Mortality of diphtheria as shown by day of injection of serum, showing number injected each day:

Cohn's Statistics.	Mortality Percentage.
Injected 78 on first day	1.3
Injected 361 on second day	11.1
Injected 284 on third day	16.5
Injected 101 on 4th day	24.7
Injected 176 after	22.7

Rolleston's Statistics.	Mortality Percentage.
Injected 62 on first day	0
Injected 324 on second day	3.1
Injected 391 on third day	6.1
Injected 309 on fourth day	10.6
Injected 203 on fifth day	12.8
Injected 211 on sixth day or after	10.9

Kosel's Statistics.	Mortality Percentage.
Injected on first day	0
Injected on second day	4
Injected on third day	13
Injected on sixth day	53

Ganghofner's Statistics.	Mortality Percentage.
Injected on first day	0
Injected on second day	8.4
Injected on third day	14.2
Injected on fourth day	17.

At Heubner's clinic in Berlin there were 40 deaths due to diphtheria between 1900 and 1910:

Heubner's Statistics.	Mortality.
Injected on the first day	0
Injected on the second day	3 deaths.
Injected on the third day	9 deaths.

It is safe to **conclude** that:

1. The prognosis of diphtheria is favorably influenced by antitoxin.
2. Antitoxin influences local diphtheritic deposits favorably, the earlier it is used.
3. If used early there are no advances of the disease to the larynx.
4. The energetic and early use of antitoxin will save many lives in the presence of laryngeal stenosis, unless the cases are malignant.
5. The use of antitoxin adds materially to the chances of intubated and tracheotomized children and adults.
6. Antitoxin cures the croup of measles.

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VII. Pneumococcus Infection

Lobar Pneumonia

(Pleuropneumonia, Lung Fever, Croupous Pneumonia, Fibrinous Pneumonia, Lungenentzündung)

The most frequent expression of the systemic infection due to the pneumococcus is *lung fever*—lobar pneumonia. It is a general infection usually associated with febrile disturbances, in which large portions of one or both lungs are involved in a croupous inflammation, due as a rule to the pneumococcus of Sternberg and Fraenkel, though croupous pneumonia may be the local expression of other general bacterial contamination. *Bacteremia, toxemia, pulmonary consolidation with consecutive obstruction and cardiac asthenia, form the complex which demands attention and influences the prognosis of the disease.* The prognosis is materially influenced by the occurrences of double or multiple infections, and the further fact that the bacteriology of many of the acute infections which often complicate pneumonia is unknown or uncertain (Pye-Smith).

As soon as it was fully understood that pneumonia is only the local expression of a general disease, a step forward was taken which has had a powerful influence on prognosis, more particularly the prophylaxis of the disease. Sir Herman Weber in England (1869), Juergensen in Germany

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(1876), and Austin Flint, Sr. (1877), in the United States, were pioneers in establishing our modern conception of pneumonia.

Pneumococcemia

With modern bacteriologic methods the presence of *pneumococcemia is established in over 70 per cent of all cases of croupous pneumonia.* The other and leading local manifestations of general pneumococcus infection are *tonsillitis, otitis media suppurativa, meningitis, cholecystitis, endocarditis and arthritis.*

Among the most valuable data showing the influence of pneumococcemia on the prognosis of croupous pneumonia are those furnished by Dochez, from which we quote. The bacteriologic studies of the blood were made in 37 cases of lobar pneumonia. "The pneumococcus was isolated from the blood in approximately 50 per cent of the cases studied. The course of the infection in individuals with pneumococcus in the blood was more severe than in those in which no organism could be cultivated from the blood; 77 per cent of the patients with positive blood-cultures died, and 79 per cent of the patients with negative blood-cultures recovered. In fatal instances of pneumonia, where the pneumococcus was found in the blood, the number of organisms per cubic centimeter of blood was very high in the last stage of the disease. In individuals dying of pneumonia without evident blood infection, the disease was characterized by a rapid spread of the local process in the lungs!" It is believed by Dochez as the result of his observations, that the *"symptoms of collapse* developing on the fifth or sixth day of lobar pneumonia, are often the expression of serious invasion of the blood by the pneumococcus."

The *virulence of the strain* in the individual case as shown by animal experimentation and clinical experience has a direct influence on the prognosis of the disease. Rosenberger and Dorworth found that 54 per cent of their patients in whom blood-cultures showed organisms died; and 50 per cent of the patients who died showed no blood contamination. Meltzer and Lamar found that by *intrabronchial insufflation of cultures* of a very virulent pneumococcus, typical pneumonia lesions were invariably produced. These experiments gave a mortality of 16 per cent and bacteremia was present only in fatal cases. Wallstein and Meltzer experimented with *non-virulent pneumococcus;* they obtained typical consolidation of the lungs, with no mortality and no bacteremia. These views according to Meltzer, justify the conclusion which is by no means new, that *the anatomic changes in pneumonia are not the immediate cause of death, and they do not present the essential features of the disease;* "on the contrary they are manifestations of the body's fight *against* the disease." We would add that improvement and the favorable termination after crisis occur without material change in the structures involved in pneumonia;

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the heart is relieved of its burden in spite of the practically unchanged area of consolidation through which it must, for a few days at least, continue to force the blood. There is very likely in some way, at the time of crisis, a change in the character of the toxins of the pneumococcus. Cole says, that there is "a neutralization of the intoxication rather than a destruction of the bacteria existing within the body." Lees' epigrammatic remark is applicable in the consideration of our subject. "Let it be remembered that every case of pneumonia is a fight for life" to which we add, *no case is so severe that it may not recover; none so mild that it may not become serious.*

In considering the *prognosis* of pneumonia the factors which concern us most are:

1. The malignancy of the infecting organism.
2. The effect of the toxemia and the associated local lung lesion on the cardiovascular system.
3. The resistance offered by the patient.
4. The extent of the pulmonary and associated lesions.

1. The Malignancy of the Infecting Organism.—The malignancy of the infecting organism requires no further consideration. The foregoing paragraphs have proved that the prognosis depends very largely upon the virulence of the infecting strain, the result of the bacteremia and the toxemia.

2. The Effect of the Toxemia and the Associated Local Lung Lesion on the Cardiovascular System.—*This is the paramount issue in the prognosis of pneumococcus infection.* We are not dealing with the heart alone; we must consider the vasomotors, and the effect of the toxemia on both. Passler and Romberg reported a series of experiments which served to prove the relative importance in the production of the so-called heart weakness of pneumonia, of the heart itself, and of the vasomotor system. Experiments made with the pneumococcus and the Bacillus pyocyaneus, in which rabbits were inoculated, proved conclusively that the vasomotors were weakened and showed evidences of paralysis.

The prognosis of pneumonia depends largely upon the baneful influences which the toxins exert upon the vasomotor centers in the cord.

Primarily the toxemia leads to cardiac asthenia and vasomotor paralysis, to which must be added the changes in the right half of the heart, the far-reaching degenerative changes in the myocardium, the heart clots, and the mechanical obstruction in the pulmonary circuit.

The *effect of pneumococcus toxemia on heart and vessels* is malignant; but fortunately for the prognosis, it is short lived. The heart and vasomotors therefore are to be cautiously observed for prognostic data.

Blood-pressure Study.—Associated with the influence on the heart and peripheral vessels we find in blood-pressure study a prognostic index of

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great value. For reliable conclusions it is necessary to have full daily records, including frequent measurements, which positively lead to the early recognition of circulatory embarrassment.

A systolic blood-pressure much below normal in pneumonia is unfavorable; any great fall is ominous. "When the arterial pressure expressed in millimeters of mercury does not fall below the pulse rate expressed in beats per minute, the fact may be taken as an excellent augury; while the converse is equally true" (Gibson's rule).

It does not appear to us that the conclusions of Newburgh and Minot are to be accepted as proving that there is no failure of the vasomotor centers in pneumonia. Low blood pressure may not "invariably" be "of evil omen" but clinical experiences prove that *with falling blood pressure, lowering pulse amplitude and increasing pulse rate, the prognosis in all pneumonics is unfavorably influenced.*

To reach safe conclusions on this subject the pulse pressure data covering many cases and a series of years are needed, and these we have secured before framing our conclusions. Data from a small material do not justify conclusions.

Cases of *pneumonia complicated by arteriosclerosis and chronic nephritis* in which the blood-pressure remains abnormally high during a day or two, prove exceptions to the Gibson rule, and offer an unfavorable prognosis in most cases. The heart tires because of the added burden to force the blood through the consolidated lung and the obstructed arterioles.

An abnormally high blood-pressure with a slow, tense thick pulse early, is always of serious significance.

When considering the prognostic significance of some of the separate symptoms we will again refer to the pulse and heart.

3. The Resistance Offered by the Patient.—"The real predisposing moment in the case of pneumonia is to be found, not in those incidental and temporary impairments of resisting power which may occur in connection with mining work (speaking of the Rand) but in that abiding defect of resisting power which is normal to the native" (Sir Almroth Wright).

The ability of children to resist all forms of pneumonia is surprising; the prognosis during early life is usually good. The *mortality* of pneumonia during the first year of life is high, from the second year to puberty it is comparatively low, from thirty-five to forty it is high, from sixty to seventy, three-fourths of all pneumonics die. In old age, on the other hand, the disease is in many hospitals and during many seasons the principal cause of death. In old age the organs become more independent of one another than during early life; "they suffer separately, and the various lesions to which they may become subjected are scarcely echoed by the economy as a whole." In old age latency of the disease is frequent and death may be sudden and unexpected in those who were about,

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as if nothing were wrong with them. In the old as well as in the young, *the association of diseases of the heart, lungs, kidney or other separate systems, which handicap the functions of organs in any way, add enormously to the danger of pneumococcus infection;* this is particularly true of metabolic disturbances and arteriosclerosis (Elsner). The *obese* have a reduced resistance to pneumococcus infection, and melt away rapidly with symptoms of cardiac asthenia and nervous manifestations. Usually coma is a terminal symptom.

Diabetics when infected with the pneumococcus offer an exceedingly grave prognosis. The majority of these cases are atypical and present complications which add to the dangers.

The *negro* is more subject to the infection than is the white man. The inhabitants of the tropics when in their own habitations or in other climates show a decided tendency to lung inflammation and have a lowered resistance. The report to the Rand Native Labor Association recently published is intensely interesting in connection with the fatality of pneumonia among the African native, and especially the tropical native. "It was discovered that the blood-serum of whites and tropical natives has no immediate power to destroy the germ of pneumonia and that the blood of the natives does not acquire this power through either natural infection, i. e., an attack of the disease, or artificial infection, i. e., inoculation. Power to resist the growth of the pneumococci in the system is acquired, however, in some degree by inoculation." The blood of the African native, and especially the tropical native, differs from that of the European in being incapable of developing a so-called bactericidal power toward pneumonic germs, and is inferior to it in respect of its "immunizing response" or ability to produce antibodies which shall prevent the hostile germs from becoming established in the body."

Pneumonia has caused a large mortality among the African natives working on the Panama Canal; kills large numbers of laborers and soldiers (Wright) in Rhodesia, the African colonies and the Egyptian Sudan.

Pneumococcus infections represent from 3 to 7 per cent of the diseases of the civilized races. Those who live in the open air are less disposed to pneumonia than are those who live in poorly ventilated or close quarters, and they offer greater resistance when infected. The disease is more frequent among workers who are exposed to storm and wet; among these the number of victims claimed is large.

The excessive use of alcohol is a factor of enormous weight in inviting pneumococcus infection, and powerfully influences the prognosis. In our hospital we have found *pneumonia in alcoholics* among the most fatal of all diseases; the average mortality has rarely been below 50 per cent against a mortality of 10.3 per cent among the non-alcoholic patients. Alcoholics are usually neglected; they enter the hospitals or call for treat-

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ment when the disease is far advanced and are often nephritics or otherwise diseased.

Traumatism invites pneumococcus infection. Contusions of the thorax or perforation of the wall are frequently followed by traumatic pneumonia.

There are cases in which there seems to be a *predisposition*, in which pneumonia is repeatedly developed. It is surprising to note how well the disease is borne by these patients, often the type proves to be abortive, but not infrequently the patient succumbs to a second or third infection. This is particularly true of children, many of whom develop either catarrhal or croupous pneumonia with every bronchial catarrh contracted or with the ordinary infections of early life.

All experiences prove the *greater frequency of the disease among men than among women.* This is unquestionably due to the greater exposure of the former to the hardships of life and inclemencies of the weather.

The disease shows a large mortality among the *mentally defective;* the higher the grade of these, the lower the death rate.

Ziemssen many years ago called attention to the fact that the permanent inhabitants of any locality offer less resistance to pneumococcus infection than do strangers or new settlers.

We have found from a study of our material that the prognosis is more unfavorable in endemic cases where several members of a family are stricken at the same time, than in homes where but one patient is infected. In the first mentioned there is apparently greater virulence of the infecting strain.

It was formerly held that *the robust* were subject to the disease; this is not true, for we very often find pneumonia the terminal infection of many diseases, either infectious, of metabolic origin, associated with cachexias or malignant.

Pregnant women offer a strong resistance to pneumococcemia but when infected the prognosis is grave and abortion is likely to result.

Immunity following pneumonia is short-lived. One pneumococcus infection in old and young alike does not cause immunity, but tends to lower the resistance against future infection and invites subsequent attacks. Unfavorable surroundings, dust, the inhalation of gases, poor ventilation, continuous dampness, faulty nutrition, lower resistance, invite the disease, and the infected offer a more unfavorable prognosis than do those whose environment has been more favorable.

There are *seasonal influences* which influence *resistance and prognosis.* The disease is most prevalent during the winter months, the first four months of the year particularly, and it is during these months that the prognosis is least favorable.

IV. The Extent of the Pulmonary and Associated Lesions.—It may be safely concluded that in the majority of cases the extent of the lung consolidation influences the prognosis very materially; this is particularly

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true of double pneumonia. On the other hand there are many cases in which the area of infiltrated lung tissue bears no relation to the gravity of the disease. There are malignant infections which offer the gravest prognosis, in which only a limited part of one lung is involved. *It is never in any case safe to offer a prognosis from the extent of the consolidation alone.* There are always other data, which, when considered, justify a forecast of the individual case. Associated lesions, particularly thrombosis, endocarditis, pericarditis nephritis, and many others to all of which separate reference are made are powerful factors and influence our conclusions.

Temperature

Chill.—The graver infections are associated with the most severe initial chill. Two or more chills are unusual; if these recur at short intervals during the first day of symptoms a malignant infection may be suspected.

Chills are absent as a rule in children, but convulsions are not infrequent; they are not always an expression of the gravity of the pneumonia.

Severe, often repeated chills in the adult, with rapid development of the local lesion, rapid pulse, increasing evidences of heart weakness, muttering or active delirium, unfavorable facies and early evidences of pulmonary edema, are included in a symptom complex of *foudroyant cases*, in which there is prompt paralysis of the vasomotor centers and death within 24 to 36 hours. These cases are not frequent. In 14 per cent of our cases in adults the initial chill was absent. This was commonly observed in alcoholics, or in the aged and in enfeebled subjects. In the aged, without chill, the disease was of the *asthenic type*, to which reference will again be made. The mortality in these cases is very high.

In 70 per cent of our *influenza-pneumonias* there was a severe initial chill. When this occurred the disease was of much shorter duration than in those cases in which there was no chill. In some of the latter cases there were large areas of consolidation, at times remnants of recent pneumonia, without marked subjective symptoms, but in which there were positive physical signs. Most of these patients recovered completely. In many we found mixed infection, usually pneumococcus and streptococcus.

Fever.—Early high temperature in pneumonia without evidences of heart weakness is by no means unfavorable. Such cases are often of short duration and terminate by crisis on the fifth to the seventh day of the disease. The frank fever is an expression of a good reaction. *It is more favorable to have a high temperature early than after the third to the sixth day, unless at that time, it is transitory and is followed by a decided fall and profuse sweat.*

Sudden rise of temperature after the fifth day, after lysis has com-

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menced or after crisis which persists, is an indication of added complication requiring close investigation.

Under no conditions is the prognosis of pneumonia to be dependent upon the revelations of the thermometer. Such reasoning must lead to frequent error. I have seen malignant cases in which the temperature has been continuously low (101° to 102°) with marked asthenia and limited consolidation. Many of these cases ran atypical courses, were uninfluenced by treatment, the heart showing increasing weakness from day to day; some proved to be of the *migratory type* in which there were fresh exacerbations with marked *adynamia*, and most of these died in the course of 2 to 3 weeks (subacute types).

In connection with the study of the temperature, we are never to divorce ourselves from the consideration of the pulse (i. e., the heart, etc.), the character and frequency of the respirations, the mental state of the patient, the character of the sputum, to which the experienced clinician will add the *general impressions* which he receives from his survey, including facies and much which no teacher can specify, but which nevertheless becomes a factor of great value in reaching safe conclusions in many cases.

In the majority of cases in which the *temperature remains continuously high,* uninfluenced by any treatment, there are other symptoms proving the malignancy of the infection; in some of these before the end of the third or fourth day there are meningeal symptoms with possible hyperpyrexia which promptly increase, and death may follow in from 12 to 24 hours.

Fall of temperature to normal or slightly above with increase of respiratory embarrassment, cyanosis, and feeble pulse, with lowering blood-pressure and thin pink watery and profuse sputum, large and small moist râles generally distributed, is fatal in over 90 per cent of cases. In many cases there is a decided rise of temperature shortly before the crisis and in occasional cases there may be one or two exacerbations of temperature following but it is always of short duration, and convalescence is not disturbed.

Subnormal temperature continuing after crisis for from 24 to 60 hours is favorable, providing other conditions are equally encouraging.

A sudden fall of temperature, but a continuously rapid and unchanged weak pulse without a true crisis is not to be interpreted as favorable.

Prompt and complete crisis is always more favorable than is a slow lysis, for with the latter there is greater likelihood of complications.

So-called unresolved pneumonia, diagnosticated because of the persistence of fever and other symptoms beyond the reasonable period for crisis and lysis, is as a rule due to some discoverable complication; empyema, abscess, thrombosis or tuberculosis should be suspected.

Afebrile pneumonia in the aged is always serious; it is often of grippal

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origin, and may be associated with arteriosclerosis or renal complications. In these patients the blood is likely to be surcharged with urea and waste products; there is great danger of sudden heart weakness and overpowering toxemia.

There seems to be an *antagonism between pneumococcemia and uremic conditions;* when both are present, the temperature is not likely to be high, but death is usual between the tenth and fourteenth day, without marked respiratory embarrassment, but with great loss of strength and nerve force, and vasomotor paralysis.

The Circulation

I have already referred to the influence of pneumococcus toxemia on the heart and vasomotors in this chapter; *the fight for life is successful or fails in accordance with our ability to favorably influence the circulation during the active stages of the disease.* The tendency as the disease advances is toward lowering of the blood pressure, weakening of the heart muscle, paralysis of the vasomotor centers in the cord, and is often materially influenced by the mechanical obstruction in the pulmonary circuit and thrombosis of the pulmonary artery.

The paramount factor in the prognosis of all forms of pneumonia is the circulation, i. e., the heart; upon its ability to resist the effect of the pneumococcemia largely depends the fate of the patient. The association of an enfeebled heart with dilated peripheral vessels is always a serious feature. The right heart weakness depends upon the extra burden thrown upon the right ventricle by the mechanical obstruction within the pulmonary circuit and the effects of toxemia; hence the prognosis is worse when the consolidation is extensive in the presence of dilatation of the right heart and its subjective symptoms. When such symptoms develop shortly before crisis, the heart may be bridged over the critical period.

When with *weakness of the right heart,* the *liver and spleen* are enlarged and there is marked *meteorism with albuminuria, casts and reduced quantity of urine, the outlook is bad.*

Cyanosis at any stage of the disease with air hunger, hurried respirations, rapid feeble pulse, and lowering systolic blood-pressure is among the most dreaded of all symptoms.

Previous disease of the heart handicaps the pneumonic and always proves to be a factor with which we must reason in prognosis. The valvular lesions, more particularly mitral insufficiency, are more favorable than are the degenerative processes as they affect the aorta and the myocardium. Mitral stenosis and aortic insufficiency are the least favorable of the valvular lesions with pneumonia. I have piloted many pneumonics to safe convalescence and complete recovery whom I had previously treated for organic diseases of the heart including valvular, arteriosclerotic and

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myocardial changes. Much naturally depends in these cases on the associated conditions. *The rule is, that the diseased heart offers less resistance to the infection than does the normal organ.*

Persistently rapid and small pulse from the beginning, with progressively decreasing blood-pressure in the presence of constitutional and local symptoms is an expression of heart weakness. Such hearts, if crisis is early, may prove sufficient to serve through the infection but they always justify the greatest anxiety.

Increasing rapidity of the heart on the third or fourth day, with at the same time evidences of fresh invasion, hurried and unimproved respiration with scanty albuminous urine, and deep involvement of the sensorium, is a serious symptom.

Irregularity of a previously normal heart, arhythmia or intermissions before the crisis and during the first two stages of the disease, are all to be interpreted as indicating the weakening of the circulatory apparatus; with or without an alternating pulse these conditions are alarming; they are evidences of myocardial involvement.

The irregularities, intermissions, arhythmias and the erratic behavior of the heart during the period of convalescence, with a normal temperature, and relief of the inflammatory process, usually with bradycardia, while they alarm the patient and the inexperienced attendant, yield after rest and without damage. These disturbances are frequent.

Collapse during the acute stages of pneumonia is one of the dangers to be dreaded. This may be due to the sudden flooding of the blood with toxins or endotoxins, to sudden acute dilatation of the heart, pulmonary thrombosis, or embolism. Not all conditions of collapse in pneumonia prove fatal. *Timely stimulation and absolute rest saves many lives.* Often at the crisis there are associated symptoms of heart insufficiency, which in most cases are transitory.

The Respiratory System

Respiratory Symptoms.—It has been our experience that *severe pain* referable to the pleura of the inflamed lung which persists after the first 24 hours, with rapid pulse and thin bloody sputum, is evidence of a severe pneumonia. The pain is wearing, prevents sleep, robs the patient of resistance, and interferes with an already obstructed respiration.

Dyspnea per se is dangerous when it depends upon diffuse bronchiolitis, edema of the lungs, the consolidation of unusually large areas of lung tissue or myocardial weakness or degeneration, with dilatation of the right heart.

Frequency of Respirations.—With dyspnea there is always increased frequency of respiration. Marked disproportion of the pulse and respiration is always unfavorable. With a *pulse of* 110 *to* 120 *and respiration of*

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30 *to* 40 *per minute* without complications, and no other grave constitutional disturbances at the height of the disease, the prognosis is good.

Respirations of 40 *to* 50 *per minute* with corresponding increase of the pulse and fall of blood-pressure, offer a doubtful forecast.

Respirations above 50—from 50 to 70—with other symptoms of corresponding severity, are found only in malignant cases which offer but slight hope.

Rapid respirations early, and large moist and crepitant râles, and profuse watery pinkish sputum, are all evidences of pulmonary edema and promptly lead to death.

Evidences of obstruction and respiratory insufficiency which include with very rapid respiration the active playing of all accessory muscles of respiration, are always of grave import. Pye-Smith says "The bearing of the respiratory rate on diagnosis and prognosis may be summarized as follows: An increased rate due to causes local in the lungs is important in diagnosis and unimportant in prognosis; and when it is caused by toxemia, exactly the opposite is true."

Cheyne-Stokes breathing is always serious. It is evidence of deep poisoning and heart incompetence.

Hypostatic congestion of the dependent lung is an almost constant accompaniment of pneumonia. In severe and fatal cases it is fully developed, an expression of heart weakness and in turn throws an extra burden on the overtaxed organ.

Sputum.—The usual appearance and average quantity of sputum are found in the favorable cases.

Persistence of bloody sputum without improvement of constitutional symptoms, including fever and rapid pulse, demands a cautious prognosis.

Excessive and thin sputum with marked dyspnea, hurried respirations and cyanosis, is proof of respiratory embarrassment and edema, making the outlook exceedingly grave.

Orthopnea and superficial irregular respiratory movements, without ability to expectorate, large râles, noisy breathing, are evidences of the terminal stage of heart incompetence.

Cough.—The most dangerous period of pneumonia includes besides, increasing heart weakness, the inability to cough with the accumulation of exudate and secretion in the bronchi. With unrelieved pulmonary edema these patients literally drown themselves. *Free expectoration* shows the strength of the patient and is of great assistance. We have referred to the sputum in previous paragraphs, especially to the significance of the *thin prune juice pinkish sputum with evidences of edema* and again repeat that it is always a dangerous symptom.

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The Blood

Carbon Dioxid.—It has been found that "in pneumonia the diminution in the carbon dioxid content of the blood is a constant feature." "Occasional cases, however, may fail to show low carbon dioxid" (Peabody). This observer further claims: "The carbon dioxid in the blood bears little definite relation to the severity of the disease, except that it tends to be lowest in severe cases and in the terminal stages of the disease. There is less deviation from the normal in short or mild cases."

Bacteremia.—We have already considered the significance of bacteremia (pneumococcemia) on prognosis in this chapter and need not therefore repeat at this point.

Leukocytosis.—In no acute infection does prognosis depend more largely than in pneumonia on the protective powers of the blood. The assistance of the leukocytes to combat the invading army of bacteria and nullify their toxins is demanded early (*phagocytosis*).

Hekton says:

"The cure of pneumonia results from the destruction of the pneumococci in the lungs and in the blood. This is accomplished by phagocytosis and also by extra cellular digestive processes.

"The predominating general defensive reactions in pneumonia are leukocytosis and the production of antibodies for pneumococci, of which the opsonins are best known; and these appear to be specific for the group to which the infecting pneumococcus belongs."

In rapidly fatal cases Hekton says the defensive reactions are inadequate to destroy the pneumococci which persist and multiply in the lung and in the blood, while the free antibodies are absent from the blood.

In cases which offer a good prognosis the pneumococci are destroyed when "antipneumococcal reactions reach a certain height."

With lysis there is a gradual, with crisis a prompt destruction of the pneumococci in the lungs and in the blood. "In both cases, but demonstrated more clearly in crises, there is an excess of antibodies in the blood."

The leukocytic count in pneumonia offers valuable prognostic data.

With severe constitutional symptoms early and a high leukocytic count, the outlook for a favorable course is materially strengthened. Counts above 25,000 are under such circumstances encouraging.

High leukocytic counts during the entire first week are favorable. In mild infections in which there are moderate constitutional symptoms, favorable facies and physical signs, the leukocytic count of 18,000 to 25,000 considered with all that the case offers, usually justifies a favorable prognosis.

Severe infections which include marked evidences of cardiac toxemia with a low leukocytic count, possible tendency to leukopenia, offer only the gravest prognosis.

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Severe constitutional symptoms with fair heart strength, often delirium with high leukocytic count (40,000 to 50,000) offer encouragement, but the prognosis should be guardedly given.

Decrease of leukocytes with positive crisis is favorable.

Unchanged leukocytic count with pseudocrisis does not influence the course of the disease.

Rise in the number of polymorphonuclear leukocytes after crisis with febrile movement or other symptoms, is always suggestive of some complication, usually empyema, plebitis, thrombosis, abscess or other non-tuberculous process.

Suspicion of a tuberculous complication is justified with fever or persistence of physical signs, failure to convalesce satisfactorily, and a low white count. Such cases may require a number of days before positive conclusions are reached.

Conclusions.—Conclusions from the foregoing statements justify a bad prognosis in pneumonia in cases with a low leukocytic count or leukopenia.

The average mortality in cases without leukocytosis is over 50 per cent; often higher.

Cabot in 329 pneumonics found 32 with white counts of 10,000 or less; 30 of these died. The author's experiences run parallel with these figures.

The leukocytic count bears no relation to the extent of the consolidation, so far as clinicians have been able to observe.

High leukocytic counts during the first day or two with rapid decided fall following is always grave. This proved to be true experimentally by Rosenow, Williamson and others. Pneumonics showing high leukocytic counts who die, do not yield to pneumococcus toxemia directly, but to some complication such as myocarditis, meningitis, septic or pyemic disease, pulmonary thrombosis, or some other secondary disturbance.

Neutrophilic leukocytosis predominates in pneumonia; this begins with the initial chill and continues until crisis. With, or shortly before crisis, there is a decided fall in the number of the neutrophilic leukocytes. Pseudocrises do not as a rule show marked change in the leukocytic count.

Complications of inflammatory and pyogenic nature are associated with high leukocytic counts; these include abscess, empyema, endocarditis, pericarditis, phlebitis, as well as metastatic parotitis, and a variety of less frequent complications.

Eosinophilia is not present until the beginning of crisis; its appearance one or two days before crisis presages a favorable outcome (Naegeli).

Lymphocytes are relatively increased before the crisis though there is an absolute reduction of these in the blood.

The complication of ankylostomiasis by pneumonia at once reduces the existing eosinophilia. Leichtenstern found a drop of eosinophils to 6 to 7 per cent from 72 per cent. Warburg from 65 per cent to 0, and a return

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of the eosinophilia with the recovery of the patient. Acute sepsis has the same effect.

Myelocytes are found in moderately severe and grave pneumonia; they practically follow crisis (Naegeli, Türck, Schindler).

The blood-plates are always increased in numbers. The French hematologists have proved an enormous increase of platelets following crisis (Crise hematoblastique).

Fibrin is increased in the blood. Naegeli calls attention to the reduction of the fibrin content of the blood in the absence of leukocytosis.

Miller and Reed (J. A. Miller and M. A. Reed), in a study of the leukocytes in pneumonia, found in their series of 40 cases leukocyte counts varying from 15,000 to 20,000 in all cases excepting the 10 which proved fatal, in which the average of 27 counts was 21,040, while an analysis of the records of the leukocyte count in the 514 cases occurring in the 5 years—1904-1908—in the First Medical Division of Bellevue Hospital showed average counts of 20,444 for the patients who recovered, and 18,827 for those who died. From this the authors conclude that leukocytosis is as high in the fatal cases as in those which recover, a high leukocytosis indicating a very severe infection. They found also that the neutrophils vary from 72 to 77 per cent in all classes of cases excepting in the very severe infections, where they averaged 81.8 per cent. (Their study of the Arneth differential neutrophil count, in which the neutrophils are classified according to the lobulation of the nucleus, showed an increase in the fewer lobed forms. No conclusions of clinical value are drawn from this finding.)

Urobilin in the blood is probably evidence of interference with the liver function and the destruction of red blood-corpuscles; its appearance in the blood of pneumonics is unfavorable. Connor and Roper found that in fatal cases of pneumonia the bilirubin disappeared from the blood within 3 days of death and that urobilin appeared.

The coagulation time of the blood is prolonged during the acute stage of pneumonia. A return of the time to normal is favorable, and is coincident with convalescence. Dochez says, "There seems to be a simultaneous increase in the quantity of circulating fibrinogen. The lengthening of the coagulation time is probably due to an increased formation of antithrombin." This comes from the liver, and it is further held that "the stimulus to increased production of these two substances (fibrinogen and antithrombin) is due to the nature of the infecting agent."

The Nervous System

The gravest pneumococcus infections are likely to cause severe symptoms referable to the nervous system; there are exceptions to this rule.

But few cases of pneumonia pass through the acute stages without some evidences of *toxemia of the nervous system.*

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The *headache* of the early stage may often be very severe; its severity is in no way related to the gravity of the disease.

Early *delirium* is not of serious import. Muttering during sleep is usually present, and bears no relation to the nature of the infection in most cases. Wild, active delirium with failing pulse, is often evidence of deep infection; it may continue until shortly before death and in many such cases there is a large and organized thrombus in the pulmonary artery.

In alcoholics, there are almost always delirium and other evidences of alcoholic meningitis, with rapid respiration, albuminuria with casts, and death with irregular breathing in coma, after several days of the active manifestations mentioned.

Convulsions in children during the first or second days of pneumonia are not often serious; they are of grave import when they occur late and are then due to toxic nephritis or to malignancy of the infection. In the adult, convulsions during any stage of pneumonia are of serious import.

Pneumococcus Meningitis.—With convulsions and the Kernig symptom with or without positive information from examination of the lumbar fluid, pneumococcus meningitis must be suspected and an unfavorable prognosis should be given.

We have no record of recovery in which the diagnosis of pneumococcus meningitis was positively established.

Spinal Fluid (*Lumbar Puncture*).—In connection with the prognostic significance of the symptoms of meningitis with pneumonia, we consider (a) meningismus and (b) meningitis.

(a) MENINGISMUS.—Meningismus is also known as meningitis sine meningitide, pseudomeningitis, and circumscribed infectious meningitis.

The study of the spinal fluid and pathologic observations, prove that there is no "universal meningitis" in these cases but that the brain, cord and membranes are hyperemic and succulent. Here and there are small deposits of pneumococci. The spinal fluid contains an occasional polymorphonuclear leukocyte but no pneumococci. With meningismus the prognosis is comparatively good; meningitis may finally develop and change the complexion of the case. The condition is frequent in children, and at times causes the leading symptoms of brain fever in both children and adults during 24 to 48 hours before pneumonia is diagnosed.

(b) PNEUMOCOCCUS MENINGITIS.—The pneumococcus is the most frequent cause of pyogenic meningitis. The diplococcus rapidly multiplies in the membranes of the brain and in the spinal fluid. The development of symptoms is prompt and the clinical picture clear. As already intimated the prognosis is absolutely bad.

The spinal fluid withdrawn through lumbar puncture early (first 12 to 24 hours) may show no marked change, but soon (within 18 to 36 hours) there is increase of fluid, increased pressure (250 to 400 mm. and over), and albumin is found. The fluid is cloudy, it may be slightly purulent in

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occasional cases; there are many polymorphonuclear leukocytes and an abundance of pneumococci. Culture experiments prove corroborative.

Cerebral symptoms, including delirium, great unrest with mutterings in the pneumonia of the aged, is almost uniformly fatal.

Postpyrexial Delirium.—The prognosis of the *delirium following crisis, either during convalescence, or several weeks after recovery,* which we have called, *postpyrexial delirium* is good as a rule. In some cases there were no mental symptoms during the acute periods of the disease in spite of hyperpyrexia, and postpyrexial delirium followed before the end of the first week of convalescence.

The *duration* of the delirium varied. In children it continued in our cases from 2 to 5 days, in adults, aged between 30 and 45 years, from 3 to 6 weeks; in a few, with bad family histories, subacute or chronic mental disturbances developed. The latter sequel was found in our series to yield in almost all cases.

The Urinary System

Quantity of Urine.—In favorable cases the *quantity* of urine secreted continues considerably reduced, but there is not the great reduction found in the most malignant forms of the infection. In the most serious and malignant infections the quantity of the urine is reduced to but a few ounces.

Albuminuria is an almost constant attendant of pneumonia; it is not always of serious significance. Unless careful and repeated examinations are made the foregoing statement will not be verified.

Toxic nephritis shows abundant casts, marked reduction of the urine secreted, large albumin loss and the other characteristics of parenchymatous nephritis without many blood-cells. Nephritis adds to the dangers materially. *Overpowering septic nephritis* is more serious than are the other forms of kidney involvement. In all *chronic nephritides* developing pneumonia conditions of extreme gravity are presented; these include besides the cardiac toxemia, arteriosclerosis and the many associated lesions previously mentioned, upon all of which added infection can produce only baneful results.

Chlorid Excretion.—In most cases the chlorids are reduced, and return at the end of the acute stage of the disease. Increase of the chlorid content may be interpreted as being favorable.

Urea and uric acid offer no prognostic data. They are increased early, are often materially diminished before crisis, and increase within the early hours of the crisis or shortly after.

Sugar.—Glycosuria may appear during any stage of pneumonia; in cases which were normal before infection it is usually transitory and does not recur after convalescence, neither does it interfere with the progress of the case.

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With *diabetes mellitus or diabetes insipidus* the prognosis of pneumonia is exceedingly grave. Most of these cases are atypical and present serious complications. Recovery is among the possibilities.

The Skin

The prognostic significance of *herpes labialis* is debatable. There are many who interpret the vesicular eruption favorably, others offer the opposite view or claim that it is without marked significance. The weight of authority is in favor of a favorable prognosis in the presence of herpes. Our conclusion from a study of pneumonias seen during the last 7 years proves that the majority of patients with herpes recovered. This subject is still *sub judice*. No reliable clinician will ever offer prognosis based on the presence or absence of herpes vesicles.

Free sweating with decided fall of temperature at crisis is always favorable. *Excessive sweating* with cyanosis and cold extremities, pinched facies, small pulse, rapid breathing, often associated with edema of the lung is almost always fatal.

Gastro-intestinal System

Vomiting in children, occasionally in adults, does not persist as a rule and rarely interferes with the course of the disease: the same may be said of **diarrhea.**

Membranous colitis is an infrequent complication but is always serious.

Meteorism which persists is of considerable importance; it interferes with respiration, throws added work on the heart, causes great discomfort by displacing the diaphragm and frequently prevents sleep.

Hiccough is also wearing and unless controlled may increase the dangers of the infection. With alcoholics and with the asthenic types of the disease it is always ominous.

Acute Dilatation of the Stomach.—Acute dilatation of the stomach due as has been demonstrated (Fussell) to constriction of the duodenum at the root of the mesentery, with probable primary involvement of the innervation, *is one of the gravest complications of pneumonia.* When it arises suddenly during the height of the disease it may promptly lead to death unless relieved. Sudden dilatation of the stomach with chronic valvular disease and pneumonia is almost always fatal. Prompt recognition of the acute dilatation of the stomach and the use of the stomach tube will remove the dangers due to this complication.

Slight jaundice is not serious; deep jaundice with marked nervous symptoms is always grave (See Bilious Pneumonia).

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Spleen

The spleen offers no data of significance in the prognosis of the disease. It is not much enlarged; in only 35 of 100 cases was the weight above 200 grams (Osler).

Hemorrhagic infarcts of the spleen with pneumococcus endocarditis or abscess, add to dangers already grave.

Physical Signs

The prognostic significance of the physical signs referable to the consolidation must be interpreted in connection with the associated symptoms referable to the heart and vascular system separately. They offer but insignificant evidence of existing danger save in those cases where there is respiratory insufficiency with pulmonary edema and with far-reaching consolidation and atelectasis. *The dangers of pneumonia are often out of all proportion to the extent of the physical signs.*

With central pneumonia there may be overpowering toxemia before the disease can be localized by the objective and positive manifestations of consolidation.

Clinical Varieties of Croupous Pneumonia

Afebrile Pneumonia.—We have already referred to the possibility of serious pneumonia without rise of temperature. These cases may lead to crisis just as do the febrile types of the disease. The association of nephritis with such infection and the influence of uremic poisoning we have already considered in this chapter. In old patients there is reason to fear for the outcome in these cases.

Bilious Pneumonia.—In the grave cases there is deep jaundice, albuminuria with casts, reduced and concentrated urine, cerebral disturbances; these often include active delirium. There is, in most, infection of the bile passages; this may be of the mixed type (pneumococcus with either streptococcus, staphylococcus or other contamination). The added complication is a handicap. The mortality of our cases was about 35 per cent (this includes only those with deep jaundice and the clinical picture given in this paragraph).

Pneumonia of the Alcoholic.—We have repeatedly referred to the pneumonia of the alcoholic and need not repeat.

In our hospital experiences we have found that the majority of alcoholics who die with symptoms of meningitis, delirium tremens or other acute manifestations, show on post mortem examination the presence of pulmonary consolidation.

Asthenic Pneumonia.—Friedrich Müller has given a very clear clinical picture of asthenic pneumonia. In these asthenic types of the disease we find the subject reduced as a rule by previous disease; the pulse is

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weak and small; the consolidation is usually limited; there is great unrest, marked delirium and many evidences of an atypical course. There may be no initial chill, and the sputum may never be rusty. The spleen is enlarged, pericarditis and endocarditis are frequent complications. Endemic influences are paramount. These cases, because of the adynamia and the multiplicity of complications offer an uncertain, often unfavorable prognosis.

Migratory Pneumonia.—The prognosis of migratory pneumonia continues uncertain during long periods; the disease is exceedingly dangerous. There are repeated fresh invasions of lung tissue and in most there is added streptococcus infection. The duration of these cases varies. It may be 3 weeks, often longer, and occasionally the patient dies after several months of mixed infection. In some of these there is also malignant endocarditis; all with this complication die.

Embolic Pneumonia.—Embolic pneumonia is often an expression of malignant endocarditis (pneumococcus or other infection). There are wedge-shaped infarcts; the symptoms are atypical, and the prognosis is grave.

Influenza Pneumonia.—Influenza pneumonia has been fully considered in the chapter on Influenza.

Hypostatic Pneumonia.—Hypostatic pneumonia accompanies acute and chronic infections or disease in which there has been preceding hypostatic congestion. It always adds a large element of danger, and is often an expression of an *insufficient myocardium.* It is often a sequel of chronic disease in old people who have been bedridden during long periods; often ends life after fracture of the hip, after operations in the decrepit, and in chronic brain and spinal lesions.

Aspiration Pneumonia.—Aspiration pneumonia, due to the entrance of foreign substances into the lung, following ether anesthesia, or associated with paralyses—bulbar, glossopharyngeal—diphtheria, and other acute and chronic diseases, is serious if the associated condition is grave. The close study of the clinical history with the influence of the symptoms separately considered is needed to clear the horizon for prognosis.

Pneumonia and Tuberculosis.—Pneumonia complicating tuberculosis is partially considered in connection with pulmonary tuberculosis.

These cases include:

I. *Acute croupous pneumonia, in which the disease attacks an area of lung tissue,* the greater part of which is the seat of infiltrating but latent tuberculosis. The prognosis is not necessarily bad; many under favorable conditions recover.

II. Cases in which there is (a) an *acute croupous or catarrhal pneumonia in the immediate vicinity of tuberculous areas.* The disease may run its course, terminate by crisis or lysis. There is usually no hemoptysis.

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(b) *Chronic or subacute pulmonary tuberculosis* in which pneumonia attacks distant parts of the diseased or previously healthy lung, in which there is no early hemoptysis, but in which the tuberculous process is actively progressive. The prognosis of these cases is bad.

III. *Cases in which there is mixed infection* (pneumococcus and streptococcus) in which the acute pneumonic consolidation is added either to a latent or an active pulmonary tuberculosis. Hemoptysis is an early symptom of the acute exacerbation, or immediately precedes the pneumonia, the latter depending on the aspiration of infecting agents from the seat of the original tuberculous infiltration, which is usually disorganized. The prognosis of this type is bad.

IV. *Cases of acute croupous or catarrhal pneumonia with concurrent tuberculous infection.* This complex is usually found in patients with lowered vitality resulting from childbearing, alcoholism, or unfavorable environment. In these patients there is in a short time disorganization of lung tissue, cheesy infiltration, coagulation necrosis, hectic fever, and death.

Complications

The complications which influence the prognosis of pneumococcus infection not previously fully considered in this chapter are: (1) Pulmonary edema, (2) Gangrene of the lung, (3) Empyema, (4) Pleurisy (serous), (5) Bronchitis, (6) Bronchorrhea, (7) Abscess of the lung, (8) Emphysema, (9) Purulent infiltration of the lung, (10) Fibrosis of the lung, (11) Pericarditis, (12) Endocarditis, (malignant and benign), (13) Arthritis (suppurative and non-suppurative), (14) Suppurative peritonitis, (15) Otitis media suppurativa, (16) Purpura, (17) Neuritis (peripheral), (18) Metastatic parotitis.

1. **Pulmonary Edema.**—Pulmonary edema may develop early, when it literally drowns the patient in his own serum. Such cases are of the foudroyant type and die within the first 2 or 3 days of the disease. When pulmonary edema develops after the first stage of the disease, and is not promptly controlled it is among the most serious complications of pneumonia.

Pulmonary edema is always a life threatening complication. Repeated reference has been made to its association with the clinical types in the previous pages.

2. **Gangrene of the Lung.**—Gangrene of the lung is not a frequent complication. Pye-Smith reports 37 cases in 7,868 pneumonics. When extensive it is usually fatal. When circumscribed, recovery followed in several of my cases; such recoveries are always slow. Some cases lead to long periods of sepsis; loss of strength and flesh is progressive, and death occurs after several months.

3. **Empyema.**—Pneumococcus empyema offers a more favorable prognosis than do any of the other infections which may cause it.

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Children develop empyema oftener than do adults. The incidence of this complication varies with different years and with different epidemics; the statistics are therefore unreliable unless the average covers several years. Such statistics of our cases show an average of 6 per cent in our pneumonias of the past 7 years.

The *early recognition* of empyema and its prompt and radical treatment in all ages offers an excellent prognosis in the absence of other complications. This subject is fully treated in another chapter (See Purulent Pleurisy).

4. **Pleurisy** (*Serous and Fibrinous*).—Pleurisy following pneumonia is usually promptly relieved, if detected early. But few cases of lung inflammation pass to convalescence without more or less inflammation of the overlying pleura during the second or third stage of the disease. The prognosis in uncomplicated cases is good. In the fatal cases of pneumonia pleurisy is found in over nine-tenths of all cases, but is not the cause of death.

Unrecognized pleural effusion, which displaces the lung and surrounding organs during long periods in which spontaneous recovery follows, may cause permanent damage because of adhesions and consecutive interference with the functions of separate organs (See Serous Pleurisy).

When pleurisy becomes chronic, there is always danger of fibrosis of the lung, i. e., final chronic interstitial pneumonia (See Chronic Interstitial Pneumonia).

5. **Bronchitis and Bronchiolitis.**—In old people and very young children bronchitis of the smaller tubes is often a serious complication.

In adults, complicating bronchitis has less influence on prognosis than in other forms of the disease, more particularly bronchopneumonia. Most cases of croupous pneumonia have more or less bronchitis as a complication.

6. **Bronchorrhea.**—Bronchorrhea may either precede or follow pneumonia. Bronchial dilatations may harbor disease-producing organisms and lead to further complications. Many patients who have bronchorrhea seem predisposed to repeated but limited croupous or catarrhal pneumonic processes.

Chronic bronchitis with bronchorrhea may, in the presence of acute pneumonia, particularly when there is associated emphysema, interfere with the overburdened organs of respiration and throw added work on the right heart.

7. **Abscess of the Lung.**—All of our cases of superficial lung abscess in which we made early diagnosis and treated radically, made satisfactory recoveries. Deep seated abscess of the lung is not frequent and is usually fatal; many of these cases are discovered post mortem. Multiple abscesses are found with mixed (pyogenic and pneumococcus) infection, are a part of an existing pyemia and are fatal (metastatic abscesses). Abscess of

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the lung may lead to or may be associated with *gangrene,* and the outcome is grave. Superficial abscess may break into the pleural cavity, into a bronchus, into the mediastinum or pericardium. Rupture into the pleural cavity leads to pyopneumothorax. All of these accidents are serious. Abscess of the lung with *empyema* offers a less favorable prognosis than does the latter alone (See Empyema).

8. **Emphysema.**—We referred to emphysema in considering bronchorrhea with chronic bronchitis. Emphysema may complicate acute pneumonia involving healthy lung tissue, and is largely a compensatory hypertrophy; it is physiological and does not influence the progress of the primary infection.

9. **Purulent Infiltration of the Lung.**—Purulent infiltration of the lung may occur during the stage of grey hepatization. It is held by some authors to be identical patholigically with abscess (Beitzke), and by many is considered to be uniformly fatal. Pye-Smith expresses the belief "that purulent infiltration need not be fatal, but may end in complete recovery" and holds further "that it is nothing more than an acute edema of the lung in a stage of grey hepatization, and that it marks the complete arrest of the process of resolution for the time being." We have reason to believe from our experience with conditions diagnosed as purulent infiltration complicating pneumonia that the contentions of Pye-Smith are correct—that while the condition is serious, it is not necessarily fatal.

10. **Fibrosis of the Lung.**—Fibrosis of the lung following pneumonia is not frequent. The pathologic changes are identical with chronic interstitial pneumonia which is separately considered (See Chronic Pneumonia). Probably deep pleural changes which become chronic are responsible for the connective tissue overgrowth. The condition is always chronic; patients may live during many years and usually die of intercurrent disease, or tuberculization may follow.

11. **Pericarditis.**—Inflammation of the pericardium may with pneumonia be either *serous* or *purulent.* The serous effusion is less serious than is the purulent. The latter is more likely to run an acute course, the former is often subacute or may merge into a chronic state.

Pericarditis may be an early or a late complication; it is more frequent with inflammation of the right lung.

Post mortem statistics prove the presence of pericarditis in 10 to 12 per cent of the pneumonias examined. Chatard found 35 cases of pericarditis in 658 pneumonias at Johns Hopkins Hospital of which 31 died. These figures prove the great danger of the complication.

Purulent pericarditis complicating the early stages of pneumonia is almost uniformly fatal. Pneumonics who live beyond the acute stage with pericarditis and effusion offer encouragement for radical surgical treatment.

Myocarditis or myocardial degeneration is an almost constant accom-

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paniment of pericarditis adding to its dangers. *Acute dilatation of the ventricles* with myocarditis and pericarditis is a frequent cause of sudden death.

12. **Endocarditis.**—Endocarditis may be either (a) malignant or (b) benign. *Preëxisting endocarditis* always adds to the danger of pneumonia. It is at once a serious handicap for the heart; it is unfavorably influenced by the toxemia and the mechanical obstructions—conditions with which it is less able to cope than is the normal heart.

(a) MALIGNANT ENDOCARDITIS.—The diseased heart valves invite the deposit of pneumococci, acute exacerbations of endocarditis result, *pneumococcus endocarditis* develops which may run an acute or exceedingly chronic course with multiple infarcts in the various organs of the body and which in the end kills the patient. *We have not a single case of recovery of pneumococcus endocarditis to report in which the diagnosis was positively confirmed by blood cultural methods* (See Malignant Endocarditis).

(b) BENIGN ENDOCARDITIS.—Endocarditis complicates between 6 and 10 per cent of pneumonias, but a small per cent of these are of the malignant type, and the majority therefore yield to treatment. There are many associated conditions which influence the prognosis of all forms of endocarditis complicating pneumonia; among these are, as with pericarditis, the associated myocardial degeneration and vasomotor paralyses. All features must receive careful consideration before the clinician commits himself. It will always be wise to give guarded prognosis with all heart complications in pneumonia.

13. **Arthritis.**—In our experience SUPPURATIVE ARTHRITIS has been so rare as to require but casual mention. The complication is more frequent in children than in adults. One large joint is usually involved which finally suppurates. The condition is grave and leads to death in one-half of the cases, or to permanent damage to the joint. When the complication is early it is most serious. NON-SUPPURATIVE POLYARTHRITIS only occasionally complicates pneumonia; it may interfere with convalescence, rarely materially influences prognosis.

14. **Suppurative Peritonitis.**—Suppurative peritonitis is mentioned by Pye-Smith as having occurred in 22 of his 7,868 cases of pneumonia —0.3 per cent. We have never, in our experience met with a case.

15. **Otitis media suppurativa.**—Uncomplicated middle ear inflammation is a frequent complication of the pneumonia of children; but few adults suffer. When radically treated early otitis does not influence the prognosis of the primary infection. Neglected cases or those overlooked may lead to sequelæ; among thees are meningitis, septic or pyemic conditions, cerebral thrombosis, abscess of the brain and other distant disturbances.

16. **Purpura.**—Purpuric conditions which develop during the active

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stages of pneumonia are always serious. In such cases the prognosis is exceedingly grave.

Purpuric conditions which develop after the acute stages are either due to the malignant pneumococcus endocarditis (petechiæ, infarcts, etc.), or they may be an expression of a depraved blood state. If the latter condition is the cause of the symptoms, there are likely to be hemorrhages from mucous membranes and skin lesions; the prognosis is good, but convalescence is slow. When purpuric symptoms are due to septic emboli (malignant endocarditis) there are as a rule no hemorrhages from the mucous membranes, but infarcts into vital organs, including brain, kidney, spleen and lung, with characteristic symptoms. The prognosis is unfavorable.

17. **Neuritis** (Peripheral).—Multiple neuritis may complicate convalescence; it was found in few of our cases. Recovery is slow but certain. In the few cases we have seen the four extremities have been involved.

18. **Metastatic Parotitis.**—Metastatic parotitis is considered in a separate chapter (See Metastatic Parotitis).

With pneumonia it is always serious and is often associated with the more malignant infections, especially malignant endocarditis.

There are no organs of the body which may not be involved during an acute pneumonia and complicate it. To consider all of the possible complications would lead us into an exhaustive study of the entire field of pathology (Jurgensen). With the data given in this chapter the leading factors which influence prognosis are brought within the reach of the reader.

Statistics and the Results of Treatment

We quote from our article (Elsner): "Hospital statistics, which it may be assumed offer the only collective information available which shows the results of treatment, are misleading and often unjust. Neglected cases are found in all services and are numerous; many alcoholics are brought to our wards moribund; not a few cases treated from the beginning of the infection in private homes without adequate nursing finally enter the hospital wards to die. All of these cases showing a high mortality are included in published statistics, and are received by the profession and the lay world as representing the actual results of our fight against the disease.

In my recent service at St. Joseph's Hospital in Syracuse, we received into our wards 34 cases of pneumonia, of which 8 died; of this number 5 died within the first 24 hours following admission. Our published mortality was 23.5 per cent, whereas the results of treatment, or more properly, the mortality of cases receiving hospital care during more than 24 hours, presented a more hopeful picture. Of the remaining 29 cases only

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3 died, and of these, 2 were chronic alcoholics—a mortality of only 10.3 per cent. These statistics are repeated in the wards of all general hospitals year after year, and lead the thoughtful to the conclusion that the truth concerning the effect of treatment can be reached only after a thorough analysis of statistics and the grouping of cases."

It may be concluded that the rational modern treatment of pneumonia, including careful nursing, materially influence the prognosis of the disease. It is a mistake to subscribe to the ancient dictum that the healthy and active offer a less favorable prognosis than do the weak and sickly.

The Influence of Prophylactic Vaccination

It would seem that with pneumonia as with typhoid fever, we may hope that prophylactic inoculation will finally influence the frequency and the course of the disease. The observations of Sir Almroth Wright definitely proved that preventive inoculation in the Premier diamond mine only 5 per cent of the inoculated natives contracted pneumonia as against 10 per cent of the uninoculated, and that the percentage of deaths was: inoculated 1 per cent, uninoculated 3 per cent.

There are at the present time no evidences which prove that *vaccine therapy* influences the prognosis of actual pneumonia.

2. *Bronchopneumonia*

(*Insular Pneumonia, Catarrhal Pneumonia, Lobular Pneumonia, Desquamating Pneumonia, Secondary Pneumonia, Capillary Bronchitis*)

Bronchopneumonia is almost always secondary to preëxisting bronchial catarrh; it is a catarrhal inflammation of the bronchioles with characteristic changes in the parenchyma of the lung, including exudation into the air cells which is highly albuminous, usually non-coagulable, containing desquamated epithelial alveolar cells, leukocytes and few erythrocytes. The desquamated epithelium undergoes fatty and cellular degeneration as the disease progresses. The exudate fills the air cells invaded. The alveolar walls are hyperemic and are infiltrated with round cells. The fibrin content varies. In cases following measles and diphtheria in children, fibrin is often present in large amounts with the cellular elements which justify the diagnosis of *fibrinous bronchopneumonia.*

Primary bronchopneumonia is not frequent. Less than one-fourth of all cases are primary. This is probably a higher figure than would be justified if full histories were always obtainable. In children after the second year the prognosis of primary bronchopneumonia is relatively good. Younger babes show less resistance, but the prognosis cannot be considered absolutely bad (25 to 40 per cent).

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The *lesions,* in contradistinction to the lobar form of pneumonia, are lobular, multiple, and invade both lungs. Confluence of islands of disease is frequent.

Bronchopneumonia is a disease of early and of late life.

The *catarrhal inflammation* of the bronchioles of influenzal origin is frequently followed by lobular pneumonia, and has been considered in the chapter on influenza (See Influenza).

Lobular pneumonia is the characteristic inflammation of the lung which complicates diphtheria, scarlet fever, measles, whooping cough, typhoid and typhus fever, plague, bronchitis, bronchiolitis and other acute infections.

Clinical data which are fully discussed in connection with pneumococcemia and lobar pneumonia are largely applicable in reaching conclusions for prognosis in bronchopneumonia, and to these the reader is referred (See Pneumococcemia).

Complications of Bronchopneumonia

Bronchopneumonia is oftener complicated by *atelectasis* than is lobar pneumonia, and when large areas of lung tissue are collapsed, the prognosis is correspondingly bad.

The prognosis must of necessity depend very largely upon the nature of the primary disease and the other factors to which full reference was made in the Section on Croupous Pneumonia, including:

I. The malignancy of the infecting agent.

II. The effect of the toxemia and the associated local lung lesions on the cardiovascular system.

III. The resistance offered by the patient.

IV. The extent of the pulmonary and associated lesions. (For full consideration see Pneumococcemia).

Bronchopneumonia is in many cases *an expression of pneumococcus infection;* it may be of streptococcus, staphylococcus, meningococcus, micrococcus catarrhalis, influenza bacillus, diphtheritic, bacillus coli or other bacterial origin. *Mixed infection is frequent*; usually the pneumococcus is found with some one of the infecting agents mentioned in the preceding paragraph.

Pneumonic plague has been separately considered (See Plague).

The prognosis of bronchopneumonia must always depend upon the character and cause of the preceding disease or accompanying bronchitis, the virulence of the specific associated microörganism, and the nature of the inspired or aspirated substances which were paramount in causing extension of the disease.

The cases of *aspiration bronchopneumonia* are included in a separate class, and the prognosis also depends upon the cause of the entrance of the foreign and the infecting substances.

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Aspiration pneumonia with cerebral apoplexy, bulbar paralysis, diphtheritic paralysis, uremia, associated with tracheotomy or other operative measures, cancer of the upper air passages, is almost always fatal.

Bronchial hemorrhage may lead to catarrhal pneumonia; the prognosis is usually favorable.

Cases in which the exudate is hemorrhagic are associated with the most malignant infections and are always serious.

The ability of children to resist bronchopneumonia is often surprising: better after the second year than before. Obese children, those with rachitis, the syphilitic, and the tuberculous, offer reduced resistance and cloud the prognosis. Conditions in children may be extreme, the picture may appear hopeless and yet full restoration to health may follow. *Cyanosis and extensive atelectasis* are unfavorable features.

Special symptoms offer the same relative prognostic significance in bronchopneumonia as in lobar pneumonia (See Lobar Pneumonia: Pneumococcemia).

It may be added to what has been said that *early high temperatures are not to be interpreted as necessarily serious, but late hyperpyrexia is always an expression of uncontrolled disease and makes positive prognosis impossible.*

Low temperatures, i. e., 100½° to 101° F. or lower, are often an expression of weakness; are found at times in cachetic children, those who are exhausted and without resistance.

The disease in young children is of longer duration than is lobar pneumonia: it may last from 7 to 21 days. Protracted cases usually die. Relapse is frequent.

The Significance of the Complications

There are fewer remnants of disease and complications than in lobar pneumonia. The significance of the few which are found may be studied in the chapter on lobar pneumonia.

Septic lesions are rare after bronchopneumonia.

The *bronchial nodes* are often enlarged; they may become tuberculous or they may, as has been repeatedly suggested in the consideration of pulmonary tuberculosis (See Tuberculosis), hold a latent focus during many years which may finally lead to active disease.

The prognosis of pneumonia is less favorable in children with measles, whooping cough, diphtheria and scarlet fever than in those who had simple bronchitis of the larger bronchi before the lung infection.

Our *mortality* in private practice in children is not above 10 per cent. In hospital practice it is much higher, 12 to 30 per cent.

Aspiration, ether pneumonia and pneumonia in children following the entrance of foreign substances into the lung are all exceedingly grave diseases.

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The approach of bronchopneumonia may be expected in children when in the midst of an acute infection associated with bronchitis the respirations are suddenly increased, there is increased movement of the respiratory and accessory muscles, the temperature shows a decided rise, and the pulse is correspondingly accelerated.

In the aged bronchopneumonia is one of the most frequent causes of death. Statistics are of but little value because the primary conditions are often so serious that it is difficult to determine accurately their relative importance in the prognosis of separate conditions. It may be assumed, however, that in the aged, the secondary bronchopneumonia is the terminal complication which hastens death (See Influence of Age, etc.; chapter Pneumococcemia.

With *typhoid fever,* long continued *hypostatic congestion, adynamia,* and often *atelectasis,* the prognosis continues grave, and the forecast uncertain during several days.

Chronic pneumonia, bronchiectasis and emphysema are occasional sequelæ of bronchopneumonia.

Catarrhal pneumonia is more fatal than lobar pneumonia.

The more acute the course, both in children and in adults, the better is the prognosis.

The more extensive the inflammatory process, the greater is the danger to the patient.

The combination of meningitis and catarrhal pneumonia offers only the most dismal prognosis.

In reaching conclusions concerning the influence of the heart and vascular system the data given in connection with pneumococcemia should be studied.

Marked leukocytosis is favorable, but blood pictures are less reliable than in lobar pneumonia because of the influence of the primary infections in most cases.

The further considerations of the prognosis of bronchopneumonia is considered in connection with the many diseases which it may complicate in the separate chapters dealing with such diseases.

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VIII. Erysipelas

(*Die Rose, Rotlauf*)

Etiology

The Streptococcus Erysipelatis.—Erysipelas is an infectious, contagious disease caused by the Streptococcus erysipelatis, a strain of the streptococcus longus, also known as Streptococcus erysipelatos hemolyticus (Schottmüller), which gains entrance to the lymphatic spaces of the skin through an abrasion and causes local inflammatory changes, sometimes suppuration, often general sepsis and other complications. The disease is likely to recur; there is in some people a remarkable susceptibility and vulnerability which makes them ready to develop erysipelatous inflammations at short intervals, on slight cause, not infrequently when the standard of health is lowered.

Port of Entry.—*Excoriations of the skin about the nose, and an eroded nasal mucosa* are the most frequent ports of entry of the streptococcus; hence facial erysipelas is the most frequent form of the disease.

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Traumatism (surgical and non-surgical) causes fewer cases at present than before the days of antisepsis when erysipelas was feared not only by the physician but more by the surgeon and obstetrician. Hospital wards, maternity and surgical, were at times of epidemics decimated by the infection following operations and labor. The mortality in hospitals and public institutions at times of peace and during war in the past, has been alarming, reaching from 7 to 25 per cent and higher, until at present owing to modern precautions the presence of erysipelatous infection in a hospital ward creates a strong suspicion of carelessness, which cannot always be charged to the attendants but should always be recognized as a preventable complication.

Period of Incubation.—The period of incubation is short—not longer than from 3 to 4 days as a rule—though in the rapidly spreading and sthenic types of the disease it may be but 24 hours.

Complications Influencing Growth of the Infection

The more virulent and malignant cases, running a rapid course, are found in **alcoholics and those debilitated by dissipation and chronic disease.**

With **cirrhosis of the liver and chronic nephritis, erysipelas** is always a serious complication; also in the obese and those suffering from chronic heart lesions.

Puerperal erysipelas is among the most serious complications of childbirth. The mortality varies in accordance with the virulence of the infecting strain, the resistance and age of the patient, the extent of the disease and the trauma, and the ability of the vasomotors and myocardium to withstand the toxemia. It is never to be lightly regarded.

Erysipelas of the newborn (umbilical) involving the skin and umbilical cord is often associated with phlebitis and offers a grave prognosis; most babes thus infected die.

Erysipelas of the aged is always associated with great danger, greater when there is cardiovascular or renal disease coexistent. With *diabetes* and erysipelas the prognosis is almost always unfavorable.

Local Manifestations

The more extensive the local manifestations of infection, the more outspoken are the constitutional symptoms. *Tendency to migration* of skin lesions is found in the less acute cases; the course of these is often tedious and convalescence slow. Such cases often offer a serious outlook, they may complicate *streptococcus tonsillitis* due to *milk infection* or epidemics of *streptococcus infection of unknown origin.* Such a case we recently saw during an epidemic which spread over several townships in which the ini-

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tial infection was tonsillar; later there were from 6 to 8 weeks of migratory erysipelas, in which the entire surface of the body was involved at various times, with final meningitis and death.

Bloody vesicles with petechiæ and limited sloughs with other evidences of *purpura or malignant endocarditis* and *infarcts*, are unfavorable and present only in the gravest cases.

Extension to the mucous membranes of the disease with edema of the glottis may lead to *sudden death.*

Glandular enlargements in the neighborhood of the infected skin need cause no alarm.

General Manifestations

Circulatory Disturbances.—*In the active and robust with a clean previous history,* the *hyperpyrexia* of the third and fourth days in the absence of other alarming symptoms such as heart weakness, need not discourage the attendant. In these cases there may be active delirium and a rapid pulse, and yet the prognosis in over 95 per cent of cases proves to be favorable.

The *height of the temperature may mislead* the clinician in occasional cases, for he may fail to recognize the danger in the *aged or feeble,* in which there is but *slight fever* but characteristic asthenia. Such patients bear erysipelas badly.

The *pulse* is rapid according to the height of the fever and may be arhythmic at times during the first week.

Arhythmia and dicrotism with hyperpyrexia and meningeal symptoms present a complex which should cause anxiety during several days. Unless there be *purulent meningitis* or other serious complication and the disease is limited, over 90 per cent of these patients finally recover.

A *small, rapid, soft and thready irregular pulse,* with other evidences of malignancy or complications, is always alarming and should lead to a guarded forecast.

Whenever in the course of erysipelas there are evidences of *endocarditis* the possibility of the malignancy of the latter must be considered. Complicating streptococcus endocarditis offers an unfavorable outlook.

Dry pericarditis is not of itself fatal. *Purulent pericarditis* is a part of an existing pyemia or general sepsis, and is found only in the gravest cases.

Systolic mitral murmur due to relative muscular insufficiency, with or without accentuation of the second pulmonic sound, disappears during or shortly after convalescence and is followed by normal heart function in almost all cases.

Non-malignant endocarditis as a rule, when a complication, leads to the recovery of the patient, though there may be some evidences later of

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its previous existence in deformed valves (murmurs) and compensatory change (hypertrophy).

Respiratory System.—*Hurried respiration,* with or without evidences of lung involvement (pneumonia, bronchitis, etc.) has in our experience been a symptom found with malignancy and is exceedingly grave. *Rapid respiration does not always indicate the presence of pneumonia.*

Pneumonia, particularly with alcoholism, is likely to prove fatal in the presence of erysipelas.

Purulent pleurisy, associated with migratory erysipelas, has proved to be a serious complication, though not all cases are fatal.

Albuminuria is not of serious import, it is present in most cases at the height of the infection. In 10 per cent of our cases there were evidences of nephritis; among these the mortality was low. Occasionally bloody urine was found without interfering with a favorable issue.

Purulent meningitis is an occasional cause of death in erysipelas.

Metastatic parotitis (see Metastatic Parotitis), is evidence of sepsis and malignancy.

Blood.—There is, in the severest cases, *enormous albumin loss* from the blood which is in direct proportion to the gravity of the disease.

In severe cases there is *enormous destruction of red blood-corpuscles.* A count of 3,000,000 in a previously normal blood is of grave significance. *Poikilocytosis in these unfavorable cases is striking.*

Large hemoglobin loss is also an early evidence of the gravity of the disease.

Leukocytosis is usually present in cases of erysipelas, is largely dependent upon complications, mixed infections, etc.; alone it is of small prognostic value.

Conclusions

The prognosis of the average case of erysipelas is good; the *mortality* varies from 3 to 5 per cent.

The *leading causes of death* in our experience have been cardiac toxemia, purulent meningitis, general sepsis, malignant endocarditis (streptococcus), mixed infection, alcoholic meningitis and delirium tremens, sinus thrombosis, exhaustion due to repeated re-infection at short intervals. When erysipelas develops *in the midst of other acute infections,* as with typhoid and with surgical diseases, or after surgical operations, the prognosis is grave.

Our experience with *non-alcoholic patients predisposed to the disease,* who have been repeatedly infected at long intervals, has been uniformly favorable. In spite of repeated fiery attacks they have recovered. One of these is now alive, over 80 years of age, after 50 years of recurring erysipelas.

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IX. Epidemic Cerebrospinal Meningitis

(*Übertragbare Genickstarre*)

Epidemic cerebrospinal meningitis is an epidemic or sporadic inflammation of the cerebrospinal membranes due to the Meningococcus of Weichselbaum (1887); characterized by symptoms referable to the brain and cord, in which the *diagnosis can be positively verified by the presence of the Meningococcus of Weichselbaum in the withdrawn lumbar fluid.*

Mortality

There is scarcely a year when the disease fails to claim its victims in most cities and countries of the civilized world. The mortality is greatest during April and May, the number increasing during years of endemics and epidemics. Thus in a period of ten years before the introduction of the Flexner serum, there were in the city of Syracuse 175 deaths due to cerebrospinal meningitis, and 499 deaths due to non-epidemic meningitis.

Years.	Cerebrospinal Meningitis.	Non-epidemic Meningitis.
1893	11	55
1894	4	61
1895	17	61
1896	18	51
1897	12	51
1898	19	71
1899	45	43
1900	13	29
1901	9	23
1902	19	32
1903	8	22
	175	499

In the city of New York the number of deaths from cerebrospinal meningitis from January 1894 to November 1904 was 3,189—the highest mortality was due to the prevalence of the disease in epidemic form during 1904 and 1905.

Year.	Deaths, Cases.
1894	213
1895	204
1896	178
1897	232
1898	258
1899	287
1900	201
1901	201
1902	210
1903	195
1904 (January 1 to November 1, 1904)	1,010
	3,189

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STATISTICS OF THE CITY OF NEW YORK SINCE 1904.

YEAR.	CASES REPORTED.	DEATHS.
*1904	482	1,403
1905	2,755	2,025
1906	1,032	812
1907	828	642
1908	380	316
1909	346	326
1910	242	191
1911	266	224
1912	250	196
1913	232	202

* 1,010 cases included in previous table would leave 393 deaths of the 482 reported.

The disease claims the larger number of its victims from the homes of the poor, though the disease may exist under favorable conditions and in sanitary homes. During epidemics, the *limited number* of cases and the *absence of continuous extension* are often surprising, as was also the high mortality, before the introduction of the present method of treating the disease. The disease is often held within a narrow precinct of a city or a corner of a township.

When epidemic meningitis visits country districts the same remarkable *limitation of its ravages* is noticed in the small number attacked. These facts are well illustrated by an experience on board the U. S. receiving ship Minneapolis, as reported by Surgeon Stokes. The ship was overcrowded with 1,450 men on board at the time of the outbreak, yet only 23 cases developed; of these 6 died—an unusually low mortality of 26 per cent.

Clinically and experimentally it has been demonstrated that *pneumococcus, influenzal and other forms of cerebrospinal meningitis are more virulent than are those of epidemic origin due to the meningococcus. Pneumococcus meningitis* is almost uniformly fatal. Of 68 cases, 61 died during the first day of the disease, while Netter who reports these figures, says that only one-third of his meningococcus cases died. Huebner says "the benign nature of the meningococcus as compared with the virulence of other meningitis-producing germs, accounts for the comparatively few cases during epidemics, their ready control with the subjugation of the germ."

Occurrence

Flatten's statistics corroborate the data which I collected in New York State (Elsner), and prove that the disease is rare after the fortieth year. *Flatten's statistics,* gathered during 1905-1907 in Kattowitz, showing ages of patients, are as follows:

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0	to	5	years	559	cases
5	to	10	"	248	"
10	to	15	"	72	"
15	to	20	"	47	"
20	to	25	"	15	"
25	to	30	"	14	"
30	to	35	"	7	"
35	to	40	"	3	"
40	to	45	"	2	"
45	to	50	"	2	"
50	to	55	"	5	"
55	to	60	"	1	"
60	years and above			0	"

I found that when the disease did occur in adults, it was often invited by long continued worry and mental strain.

Sporadic cases run much the same course as do those of epidemic origin; there are no differential features.

Bacterial and cultural tests only, give the information which insure safety and the protection to which the public is entitled.

Second attacks of the disease are not likely to occur. Councilman (quoted by Elsner), found but five cases in which the disease did repeat itself in the same patient. Oppenheim does not believe that one attack gives immunity.

Factors Influencing the Severity

General Symptoms.—There are *unexplainable factors which modify the severity of* both the *epidemic* and *sporadic* disease during different years and influence its course. All degrees of severity are found with both.

For purposes of *prophylaxis* and *prognosis* it cannot be repeated too often that *the same bacteriologic cause is paramount in both epidemic and sporadic cases.*

Early *coma* or its persistence after the end of the first week is an unfavorable symptom.

Early glycosuria with coma or with marked delirium is unfavorable.

Deafness is not to be considered among the ominous symptoms so far as life is concerned. It is present in a large proportion of cases and leads to permanent deafness in from 15 to 25 per cent of cases.

Suppurative ophthalmia, panophthalmitis with perforation, is found in severe cases with mixed infection (4 to 5 per cent).

Optic neuritis is a serious complication, present in 17 per cent of Jochmann's cases, and in those who recover often leads to blindness.

Unfavorable conditions are persistence of coma, involuntary discharge of urine and feces, rapid emaciation, increasing tympany, hyperpyrexia, rapid small pulse, sudden heart weakness with subnormal temperature.

The *facies* of the patient, unlike any other disease, not easily described,

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offer a picture which impresses the clinician at once and from which he can promptly reach conlusions for prognosis.

The *pulse* and *temperature* offer nothing characteristic other than the acceleration of the former and the elevation of the latter. As death approaches the pulse becomes exceedingly rapid—due to vagus paralysis.

Hyperpyrexia with rapid pulse is usually a fatal combination.

The *urine*, usually secreted in good quantities, may be *albuminous*, and *glycosuria* is not uncommon. The former is not serious; the latter with high fever and deep invasion of the sensorium does not justify a favorable forecast. *Not all cases with glycosuria die.*

The *knee jerk* is absent in one-sixth of all cases. In one-tenth this phenomenon is absent to return as convalescence approaches. The variation in the behavior of the reflexes in different cases proves that these follow no rule and offer little for prognosis; the sensorium is often so profoundly involved as to make the tests valueless.

Striking, extreme opisthotonos with marked muscular rigidity is always an evidence of active and serious meningitis. The relief of muscular rigidity and included opisthotonos, with brightening of the mind are always encouraging.

Marked *cutaneous hyperesthesia with or without the Kernig symptom,* is always suggestive and is most pronounced in serious cases.

Herpes facialis unusually frequent and profuse in Germany, is less frequent in the United States than are the *erythemas and purpuric eruptions* (petechiæ, etc.). Herpes is of no prognostic value. Petechiæ are more ominous.

Large *cutaneous hemorrhages and bleeding from mucous membranes* are evidences of malignancy.

Early convulsions in children are not always of serious import; their persistence however is always grave.

Tonic spasm limited, without full convulsions, is characteristic of the early stage of *"postbasic meningitis."* (Lees and Barlow). These should all be considered cases of cerebrospinal meningitis and offer a bad prognosis.

Trousseau's macule is neither of great diagnostic nor prognostic value.

There are but few data referable to other organs, including kidney and spleen, which stand out as prognostic aids. Albuminuria is frequent, not significant; nephritis is rare, the spleen is not materially enlarged.

The *Kernig symptom* is an early manifestation; it is as early as opisthotonos and is late to disappear. It is present in between 90 and 95 per cent of all cases of epidemic cerebrospinal meningitis. *The persistence of the Kernig phenomenon* is of considerable value in diagnosis and prognosis in cases where the correct diagnosis was not suspected during the first week of the disease. As a rule, it is not needed to make the diagnosis; it is found with all forms of meningitis. If it persists, it should always lead

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to the suspicion of cerebrospinal meningitis and for safety, the spinal fluid should be examined bacteriologically.

Foudroyant Cases.—There are foudroyant cases in which the victim is suddenly overpowered; coma and malignant toxemia are prompt; and death may follow in the course of from 12 to 48 hours before the diagnosis can be made. We see fewer of these cases now than formerly, but occasionally they are encountered, usually early, or at the height of the epidemic. Hyperpyrexia has been a bad feature of some of these cases.

Sudden death in the midst of cases in which the prognosis has been held *sub judice,* is not infrequent. Such cases we have all met in the past and it is unjust now to charge these to the use of the serum or to any form of treatment. We have no definite cause to assign for some of these deaths, but would in explanation, quote Tourdes: "The disease is distinguished by the slowness of its cure and the rapidity of its fatal issue." This dictum was advanced during the period preceding the introduction of the Flexner serum.

Cases also foudroyant, *meningitis siderans,* are among the more fatal, and run their course unless controlled by treatment in from 4 to 6 days. If these patients finally recover, there are positive evidences of improvement after the second or third day. The sensorium gradually clears; temperature which is usually high shows decided remission; the cutaneous hyperesthesia is less; and the pulse shows increasing tone. With these changes, the blood picture and character of the lumbar fluid is also changed. Opisthotonus and rigidity, as already mentioned, are materially relieved also.

In all cases of the disease the prognosis is not encouraging if improvement is not decided before the end of the second or early in the third week.

The addition of other acute infections is always unfavorable, more particularly pneumonia, scarletina, endocarditis, pericarditis and pleuritis.

The *interstitial myocarditis* (toxic) of foudroyant cases adds enormously to the danger. The *tonsils* harbor meningococci, and from this port of entry the infection is often spread. The normal nasopharynx is antagonistic to the onward march of the Weichselbaum diplococcus.

Chronic Cases.—Chronic cases with purulent deposit in the ventricles of the brain, bathing the cord also may persist during from 4 to 6 weeks—even longer—with marked symptoms, including rigidity, Kernig symptom; the sensorium may clear; some symptoms including fever may also improve, but with persistently high pulse, increasing weakness, final return of fever, and aggravation of all conditions, (mental and physical) these patients, usually neglected from the beginning, die.

It is not at all unusual to find so-called chronic and *subacute cases* gradually mend, and in the end make full recoveries. Some of these however escape with sequelæ which handicap them throughout life. The chronic cases may end in hydrocephalus.

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Progressive hydrocephalus dependent on epidemic meningitis is among the most unfortunate and fatal sequelæ of the disease. In these cases the disease may continue during weeks—not infrequently months. Changes are found in the ependyma; there is a persistence of meningococci in the ventricles of the brain, "in much diminished numbers and of reduced virulence" (Koplik). As already stated the chronic cases, i. e., hydrocephalus, may present a clear lumbar fluid; meningococci may appear to be absent, but cultural tests show their presence.

The *marked emaciation* of these patients is characteristic and has claimed the attention of all clinicians; they look like reconcentrados when next to each other in the hospital wards. The prognosis of these cases is bad, and when they do recover a variety of *sequelæ may follow besides those already mentioned,* including permanent mental alienation, persistent cephalalgia, vertigo, loss of memory, ataxia, contractures, etc.

Abortive Cases.—Abortive cases end in the course of a few days favorably, after but few symptoms and without sequelæ. Most of these cases are found late in epidemics of the disease.

Blood Picture.—The blood picture of epidemic cerebrospinal meningitis offers valuable data for diagnosis and prognosis. Rusca has made a very extensive study of this subject. During the early stage in all cases, there is marked leukocytosis (10,000 to 45,000); polymorphonuclear increase is greatest, while the behavior of the lymphocytes is not always the same; in some cases there is increase, in others a reduction.

As the disease advances and where the condition is serious, there is at once an increase of neutrophilic leukocytes; improvement of acute conditions is at once followed by a decided fall.

There is *lymphocytic increase* with each improvement or favorable turn of the infection, whereas a decided fall is promptly noted with added complication of serious moment.

Curtius and Rusca agree that the blood picture of cases with *measle-like eruption* proves the contention of the former, that such cases offer a favorable prognosis.

Hemorrhagic exanthemata offer an unfavorable blood picture and are often foudroyant.

Returning *eosinophilia* is always favorable and is found during convalescence. Eosinophilia is usually absent in serious and malignant cases, and is never present during the terminal stage of cerebrospinal meningitis; the latter statement is true also of mast cells.

The blood picture of cerebrospinal meningitis is of greater prognostic than diagnostic value; for the latter, we must always rely upon lumbar puncture.

Lumbar Puncture.—Lumbar puncture gives positive diagnostic information as well as valuable prognostic hints.

The *fluid* in average cases is cloudy, and escapes under abnormally

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high pressure. Where there is purulent and thick effusion, the first few drops may be thick—"pussy"—after which the fluid is thinner, but remains milky or clouded. If there is acquired hydrocephalus and the condition is advanced to the subacute or chronic stage the fluid may be clear, but still the pressure is high (180 to 220 mm.). The fluid usually offers positive bacteriologic and cytologic evidence. The *centrifugalized fluid* shows abundant polymorphonuclear leukocytes and lymphocytes. With a negative result (bacteriologically) and the absence of meningococci with positive symptoms of cerebrospinal meningitis, repeated examinations of the fluid are necessary, and will lead to the correct diagnosis. It is not uncommon to find the first examination negative, the second positive.

Herter placed himself with those who believed that "lumbar puncture, more particularly the appearance of the cellular exudate in the early stages of acute cerebrospinal meningitis" is of prognostic significance. "The presence of degenerated leukocytes, containing few microörganisms while many cocci are seen to be extracellular, points to feeble powers of resistance on the part of the leukocytes and hence to a bad prognosis." It is further held that the persistence of well preserved leukocytes, showing many intracellular diplococci (indicating active phagocytosis) and the absence of many extra cellular microörganisms, indicate good powers of resistance and a better prognosis (other conditions being comparable) than in the former case." Jochmann makes a suggestion, which seems important: that in suspected cases in which the first lumbar puncture fails, bacteriologic examination of the pharyngeal content will be likely to show the presence of the meningococcus.

The *presence of sugar in the cerebrospinal fluid* may prove of some diagnostic and prognostic value in both cerebrospinal meningitis and tuberculous meningitis. This subject has received considerable attention of late, more particularly from Jacob and Connall. The latter gives the results of the examination of the cerebrospinal fluid for sugar in 133 cases of cerebrospinal meningitis, all stages of the disease included. He concludes that sugar is absent from the fluid during the acute stages of the disease. During the chronic periods sugar is present. "It may be said, however, with certain reservations, that the reappearance of the sugar is an indication that the disease is in process of cure." Jacob agrees with Connall that "in cerebrospinal meningitis sugar is absent (from the fluid) in the acute stage, but may return in some degree as the infection recedes."

Complications.—Mixed infection with either sporadic or epidemic cases is frequent; the meningococcus may have abundant companionship before death or recovery. This is always serious.

Cases of *cerebro-spinal meningitis with pneumonia* offer only the most doleful forecast.

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Meningococcus pneumonia may complicate cerebrospinal meningitis. In the presence of both of these conditions, i. e., pneumonia and cerebrospinal meningitis, the meningococcus is present in 80 per cent and the pneumococcus in 20 per cent of cases (Elsner quotes Councilman, Mallory and Wright).

Metastatic joint changes were found in a number of our cases, and *when present early aroused suspicion of arthritis and pyemia.* In one of our cases a woman, age 24, presented with arthritis limited to both ankles and profound meningococcus infection; she died in the second week of the disease. These cases are usually of mixed origin and demand a cautious forecast.

Deafness often follows otitis media suppurativa, though the labyrinth may be involved without a single auditory symptom, until the patient awakens, or days after the beginning of convalescence it is noticed that the hearing is growing gradually less acute. In some cases patients lift themselves from the acute delirium or period of unconsciousness with defective hearing, from which they may never recover. A large number of deaf mutes are found to have had epidemic cerebrospinal meningitis. Moos, quoted by Ormerod, found of 64 convalescents from cerebrospinal meningitis that 38 were deaf mutes; 20 were absolutely deaf, and 32 had a staggering gait.

Both *blindness* and *deafness* offer a bad prognosis for return of function if improvement is not prompt. *Persistence beyond 3 months of symptoms without improvement argues strongly against restoration later.*

The Influence of the Flexner Serum on the Prognosis of Meningococcus Cerebrospinal Meningitis

There never will be a time when the prognosis of the disease will fail to be influenced by the *virulence of the infecting agent.* In spite of this fact, which has been discounted in the impartial consideration of the results obtained, the profession is agreed that the *Flexner serum is a remedy of undoubted value and that it has reduced the mortality of the disease, from 70 to 25 per cent.* Indeed in some epidemics before the use of the serum, the death rate was 80, and it has been above 90 per cent. In some epidemics in which foudroyant cases were common 95 per cent died. Oppenheim reports in one epidemic (Silesia) 3,102 cases with 1,789 deaths. Koplik says "the Flexner serum has given the disease a prognosis in epidemic periods equal to that of lobar pneumonia, and in sporadic cases even a better prognosis than the pulmonary affections." He says further: "In sets of sporadic cases the outlook is not worse than in any of the ordinary affections of an infectious nature in childhood."

The prognosis during early life will continue to be influenced by the difficulties of early diagnosis and respiratory complications.

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The delay of a single day or even 12 hours in very young children is often fatal (Koplik). Koplik in a series of 400 cases collected by him found a mortality of 50 per cent in 22 patients of 1 year and below, 42 per cent between 1 and 2 years. In Koplik's service at Mt. Sinai Hospital, of 15 patients below 1 year, 10 died—66 per cent; of these 15, 2 injected on the fifteenth day recovered and 1 injected the seventeenth day was discharged improved, 1 on the twenty-first day was cured, as was 1 injected on the twenty-ninth day. 1 injected on the third day died. Of 12 patients between 1 and 2 years of age injected, 6 recovered (50 per cent); 1 of these injected on the second day of the disease died after an illness of 14 days.

Among the *causes of failure,* virulence of the infecting strains, closure of the foramen of Magendie, adhesions preventing the entrance of the serum from the cord to the subarachnoid space above, late lumbar puncture (diagnosis), are included.

Flexner's statements are always concise and are accepted as absolutely reliable. We find in his report of 1,295 cases in which intraspinal injections of his serum were given, 70 per cent of recoveries. In those injected within the first 3 days of the disease the mortality was but 18 per cent; injected between the fourth and seventh day, the mortality was 27 per cent, and those injected later 36 per cent. 125 children less than 12 months' old were injected, and 50 per cent were saved. *Of these, 5 were injected early and all were saved.* "Reduction in mortality of cerebrospinal meningitis due to the serum is from two-thirds to three-quarters of the average percentages occurring in the same periods and places among patients not subjected to the specific treatment" (Flexner). These figures tell their own story. Besides the enormous saving of life by the serum, we must add that by its use, the *course of the disease is shortened and its sequelae are limited.*

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X. Whooping-cough

(Pertussis, Keuchhusten, Coqueluche)

Whooping-cough is an infectious contagious disease of early life, due probably to the Bordet-Gengou bacillus; it is characterized by catarrhal inflammation of the respiratory tract, a paroxysmal cough, and a "whoop" which is a long-drawn inspiratory movement coming at the end of several separate convulsive coughs. The disease occurs in *epidemics* usually, but is also *sporadic;* such unexplained infections are not infrequent and occur in all communities.

Most children have had pertussis when they reach their tenth year. *One attack usually produces immunity. Female children* are always attacked in larger numbers than are males. *Cold weather* seems to invite the disease; complications are then more frequent than during warm weather. *Negro children* show a much larger fatality when infected than do whites.

Uncomplicated whooping-cough leads to recovery after passing through three stages, unless as rarely happens, the case is of the abortive type:

1. Catarrhal stage.
2. Spasmodic stage.
3. Stage of recession (decrementi).

Pertussis is the cause of many serious complications and deaths.

While the disease, *per se,* as already suggested offers an almost uniformly good prognosis, its *sequelæ make it an infection to be feared,* and one which stands out in bold relief as a leading cause of death in early life. "It exceeds diphtheria and scarlet fever in gross mortality" (Osler). The *average duration of whooping-cough* is between 6 and 8 weeks.

In children less than 2 years of age the prognosis is exceedingly grave, because of the complications. *Infants* suffering from rachitis and syphilis, or other constitutional disturbances, are prone to develop serious complications with whooping-cough because they offer but little resistance.

The *average mortality* of whooping-cough is between 5 and 6 per cent. Voit reports a mortality of 25 per cent during the first year of life in

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whooping-cough; from 1 to 5 years, 4.8 per cent; and from 6 to 15 years, 1.1 per cent.

Complications

Unfavorable surroundings invite complications and add enormously to the dangers of young children.

Convulsions at any time during the course of whooping-cough are of serious import and unless due to errors of digestion, trivial or transitory causes, are ominous. When convulsions are due to sudden cerebral lesions (cerebral hemorrhage, tuberculosis, thrombosis), the prognosis is as a rule unfavorable. To these latter complications, we will again refer.

Children who have *enlarged lymph nodes* need to be protected against all fresh infections, particularly pertussis and measles; for with these added diseases, there is always danger of complications, and with lowered vitality, *tuberculization* is to be feared.

The *most serious and numerous complications* of whooping-cough are the catarrhal inflammations of the respiratory tract, the invasion of the bronchioles and air cells, causing bronchopneumonia. *One-seventh of all cases of bronchopneumonia of early life are secondary to whooping-cough.*

It is often surprising to note the enormous *resistance* of children in the presence of far-reaching bronchopneumonia. During several days no forecast of value can be offered in the individual case. During this period children may continue desperately ill, and in spite of a complex of symptoms, which in the adult would warrant an unfavorable prognosis, they make happy recoveries. We have learned never to give up a child with bronchopneumonia for we have been agreeably surprised in cases where there seemed to be but the faintest glimmer of hope. These cases of bronchopneumonia are always secondary and are due to *mixed infection* as a rule (pneumococcus and streptococcus).

Hyperpyrexia with *rapid heart action* and symptoms referable to the *nervous system* in the presence of bronchopneumonia are always grave, and demand the greatest circumspection before a prognosis of any value can be offered.

The youngest children are most likely to contract pneumonia and other complications. Nurslings offer a high mortality with pneumonia (95 per cent), and when attacked promptly die. When in the midst of whooping-cough *fever* develops, with *increased respiration* and the *pulse correspondingly rapid, respiratory complications are to be expected;* with such symptoms bronchopneumonia is most frequent. *Rachitic children,* those who have *tuberculous* ("scrofula") *tendencies in the presence of secondary pneumonia,* as in uncomplicated whooping-cough are non-resistant; in these, the mortality is very high.

The *duration* of bronchopneumonia depends on the *frequency of relapses,* which are common and are due to fresh insular invasion.

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Tuberculous complications with pertussis are surprisingly frequent, as has been proved by post mortem examinations; the *bronchial nodes* are the most frequent seat of deposit. In these cases there are often long periods of fever and relapsing bronchopneumonia; or in occasional cases children recover with latent deposits.

Pulmonary tuberculosis is also frequent in those who die of whooping-cough. Neuroth makes the unqualified statement, that "tuberculous disease of the lung is practically never absent in children who have died of whooping-cough." *Latent deposits following whooping-cough* may become active years after the acute stage and may lead to death (See Tuberculosis).

Chronic cough, due to *bronchiectasia,* may continue during many years; may or may not be complicated with tuberculosis—making prognosis doubtful.

Emphysema which may be present during the stage of spasm usually disappears without causing damage to lung tissue.

Lobar or croupous pneumonia is not sufficiently frequent to demand consideration.

Increased intravenous pressure and associated nutritive *changes in the walls of the blood-vessels* may cause hemorrhages into the conjunctiva, from the nose, mouth, bronchi, ear, or into the skin during the paroxysmal stage—all of which are transitory and do not often influence the prognosis unfavorably.

Influenza complicating whooping-cough adds an element of danger; complications are more likely to follow, and pneumonia is foremost among these. The same is true of the influence of other added infections (measles, diphtheria and varicella).

Dilatation of the heart with moderate *hypertrophy of the left ventricle* may result in cases where paroxysms are severe and frequent; but these conditions yield after convalescence and sufficient rest. Only rarely have heart lesions in the previously healthy been the cause of sudden death.

Convulsions due to trivial or transitory factors in uncomplicated cases have already been mentioned; when convulsions are due to complications leading to organic and central changes, the prognosis is exceedingly grave.

Cerebral hemorrhage offers an unfavorable prognosis; it may lead to death or to permanent paralysis.

Hemiplegia may improve but does not as a rule disappear entirely.

Paralyses of central origin lead to permanently reduced function in most cases; though marked improvement may follow, life itself is uninfluenced. When paralyses are *associated with bulbar symptoms* the prognosis so far as life is concerned is bad.

Ocular hemorrhages usually yield, only rarely is sight permanently affected.

In occasional cases, *spinal complications* include symptoms of mye-

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litis, poliomyelitis, Landry's paralysis; in all the prognosis is the same as in the uncomplicated diseases of the nervous system. *Constitutional disturbances,* anemia, chlorosis, asthenia, chorea and faulty digestion following pertussis all yield under rest and rational treatment.

Blood

Cima found whooping-cough, as the result of his investigations of the blood, associated with *leukocytosis* very early in the disease (18,000 to 22,000). The higher the leukocytic count the more severe the disease. The youngest children show the greatest increase of leukocytes and those cases in which there are mixed infections and complications. Other data offered by the blood are of no value for prognosis.

Conclusions

A history of whooping-cough is more frequent in choreic than in other children.

In considering the prognosis of whooping-cough we are conscious of the fact that there are with this, as with all other infections, *marked differences in the virulence and character of separate epidemics; that children react differently to the infection,* that *seasonal influences* are of paramount importance, and finally that *environment,* as already suggested in this chapter, is a factor of the greatest prognostic significance. Trousseau believed that the prognosis of whooping-cough was enormously influenced by the *number of paroxysms* and concluded that more than 60 daily, justified a bad prognosis.

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XI. Gonococcus Infections

(*Gonococcemia, Gonorrheal Sepsis*)

It is not within the province of this work to consider the prognosis of local changes in the urethra, vagina, or in the eye, caused by gonococcus infection.

There are occasional septic conditions which are dependent upon the entrance of gonococci into the blood, in which there are prompt evidences

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of constitutional disturbance, and to these we refer in considering the prognosis of gonococcemia. The most frequent clinical pictures include

1. Gonococcus endocarditis.
2. Gonococcus arthritis (gonorrheal rheumatism).

1. Gonococcus Endocarditis

Ahmann, Thayer and Lazear were among the first to isolate gonococci from the blood in gonorrheal endocarditis.

The *clinical manifestations* of gonococcus endocarditis are variable. We have referred to this subject in our consideration of septic conditions, also with malignant endocarditis (See Septic Endocarditis).

There are cases which are not associated with joint symptoms; these are in the minority.

As a rule there is *monarthritis;* there may be *polyarthritis.* Soon the physical signs of endocarditis are added.

The disease may be either of the (a) typhoid, (b) pyemia (intermittent), or (c) irregular type.

(a) The Typhoid Type.—In the typhoid type the fever is continuous with slight morning remissions. The *appearance of the patient is characteristic of the typhoid condition.*

Physical signs are positive, both sides of the heart are often involved; the right side oftener than with rheumatic or non-malignant endocarditis.

The *pulse* is rapid and feeble, the *sensorium* is more or less disturbed; in some cases there is wild, in others, low muttering delirium; albuminuria is almost constantly present, which often denotes septic nephritis.

(b) Intermittent or Pyemic Type.—Occasionally the typhoid type merges into the intermittent after a day or two; sometimes there is a longer afebrile period; after a period of intermittent fever following, there may be a return to the typhoid state.

Gonorrheal endocarditis of the intermittent or pyemic type is likely to be of longer duration than is the typhoid type. With intermittent fever the periods of remission vary.

In some cases the periodicity of an intermittent malarial fever is observed; in other cases the chills and fever recur at irregular intervals during a long period—every 3, 4 or 5 days—always with profuse and weakening sweats following, and often with delirium. The other attending conditions, including albuminuria mentioned in connection with the typhoid type, are in evidence.

There are cases in which we have been deluded by *long periods of freedom from fever and other symptoms;* in such cases from 7 to 10 days have intervened without any subjective complaints, sometimes longer, when without prodromal symptoms the patient suddenly had a chill and the typical cycle followed.

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The intermittent may merge into the typhoid or irregular type of the disease. Under these conditions the usual course of the disease includes rapid exhaustion and the typical picture of septic fever, from which the patient rarely rallies.

(c) Irregular Types.—Irregular types are not infrequent with endocardial invasion. Gonococcus endocarditis may begin with irregular symptoms; the temperature may continue erratic during several days, after which the patient may fall into a typhoid condition; or the pyemic intermittent type may continue in the ascendency.

The behavior of the irregular type of gonococcus endocarditis may mislead the clinician and the gravity of the disease may not be appreciated.

Cases with irregular fever and other anomalies may include periods of varying length during which the intermittent type predominates, from which the patients fall into a typhoid condition, or there is return to an erratic and irregular behavior.

In some irregular types there is *hyperpyrexia* following a single chill which invites degenerative *myocarditis*, and death is not long postponed.

Petechiae are found in most cases of gonococcus endocarditis and are of great diagnostic and prognostic value. Their presence with the previous history of gonorrheal infection and physical signs of endocarditis clinches the diagnosis and justifies only the gravest prognosis.

Hemorrhagic infarcts into lung, brain, spleen or kidney complicate many cases. *Once the diagnosis of hemorrhagic infarct is positive, an unfavorable forecast may be given.*

The Blood.—*Leukocytosis* is a constant attendant of gonococcus endocarditis; we have failed to gain any facts from blood-counts which influence prognosis. In the more chronic and subacute cases there is increasing anemia. Our average leukocytic count was between 18,000 and 25,000. *Blood cultural methods give positive results in over 70 per cent of endocardial infection.*

Gonococcus endocarditis may follow at any time while gonococci are present anywhere in the body. In occasional cases gonococcemia follows shortly after infection; in other cases 4 weeks or even a longer time may intervene. As we have already intimated our clinical material includes no case of recovery where the diagnosis was confirmed by blood cultural methods (See Septic Endocarditis).

Recoveries have been reported by others and Jochmann contends that the prognosis of gonococcus endocarditis is the most favorable of all of the malignant endocarditis, and that recovery has followed in a few cases in which gonococcemia was positively proved by blood-cultures. The other prognostic data given in connection with our consideration of malignant endocarditis (See Septic or Malignant Endocarditis) are applicable also to gonococcus endocarditis.

Complications.—With gonococcus endocarditis, *pericarditis* and *myo-*

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carditis often occur. Pericarditis has complicated one-fourth of all cases; myocarditis many more.

Sudden and overwhelming symptoms of toxemia in cases following within 7 to 14 days after gonorrheal infection are always promptly fatal. These cases may show no endocarditis. Pneumonia, pleurisy or abscess of gonococcus origin are found post mortem in some of these.

Mixed infection complicates one-fifth of all cases.

2. *Gonococcus Arthritis*

(*Gonorrheal Rheumatism*)

So-called gonorrheal rheumatism when uncomplicated, in the absence of endocardial infection, offers a good prognosis for life; slow return of the involved joint to normal is the rule. *Permanent damage to the joint* often results, the swelling and stiffness may remain during many months, while anchylosis is a frequent sequel. Pains and swellings recur after exposure, or with the changes of the season. Cold and wet weather is unfavorable and increases all symptoms, often during months and years. *Gonococcus arthritis is always rebellious to treatment.*

Most cases are *monarticular,* the knee and ankle are the seats of predilection. *Polyarthritis* usually causes constitutional disturbances, including *fever, delirium* and at times *albuminuria. Suppuration* may follow but is relatively rare. *Relapses* are frequent, provoked by insignificant factors and recurring acute gonorrheal infection.

Most cases are chronic, even the mildest gonococcus arthritis shows remnants of invasion during months, often years, in either subjective or objective symptoms or both.

Modern vaccine treatment has seemed to modify the course of gonorrheal joint infection in some cases, but cannot be said to be a specific against the disease.

Arthritis complicates from 2 to 4 per cent of gonococcus infections.

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XII. Bacillary Dysentery

Dysentery is an infectious disease showing inflammatory and ulcerative (necrotic) lesions of the large intestine; usually *endemic* or *epidemic;* characterized by frequent bloody and mucus stools, more or less tenesmus, constitutional disturbance, and in some forms, a strong tendency to secondary suppurative hepatitis (liver abscess).

There are two varieties of dysentery:

1. Bacillary dysentery due to any one or more of three strains of the bacillus dysentericus:

(a) Shiga-Kruse bacillus.
(b) Flexner bacillus.
(c) Y' bacillus.

2. Amebic dysentery (*Amebiasis*) due to the Entameba histolytica (Loesch 1875, Koch 1883, Schaudinn). Amebiasis is considered in another chapter (q. v.).

BACILLARY DYSENTERY

General Considerations

The Bacillus.—The Bacillus dysentericus (Shiga) resembles typhoid and colon bacilli very closely, is easily cultivated, there is no sporulation, and it is negative to Gram stain.

The *several species* (Flexner, Y, and Shiga) all cause the same lesions, are morphologically similar, and all grow alike in culture media. The Flexner and Y bacilli produce *indol* in bouillon culture in a few days, the Shiga-Kruse does not. There are other differences which need not concern us in our special task of prognosis, included in differences of *agglutinations,* etc.

Occurrence and Mortality.—Convalescents, patients and the apparently well, may be *carriers* and spread the disease. It is spread by man; his *stools* are the most important factor. The future clinician will probably never have the experiences with dysentery that some who are active to-day had in the past. *Modern sanitation,* if practiced, can never again lead to such ravages as this epidemic disease has caused. Let the student of medical history familiarize himself with the data collected by Woodward which stands to-day, with clinical and pathological records as one of the most complete and painstaking medical works of the past century. Macgregor says: "In the tropics dysentery is a destructive giant compared to which strong drink is a mere phantom."

Wherever there is *overcrowding,* in camps, prisons, hospitals, asylums, during times of endemics large numbers are afflicted and in the past the mortality has been alarmingly high.

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Woodward's statistics show that during our Civil War there were 259,071 cases of *acute,* and 28,451 cases of *chronic* dysentery. To the latter number, the increasing pension rolls during the past 40 years would unquestionably add many.

Dysentery in Japan shows a mortality of 26.5 per cent.

Epidemics of dysentery in New York State (central) mentioned in this chapter in connection with malarial infection of bacillary origin, claimed less than 10 per cent of those infected.

Symptoms

The lesions which concern the clinician are an inflammation of the mucous membrane of the large intestine with strong tendency to ulceration and destruction of tissue. In some cases, there is superficial loss of the mucosa with diphtheritic deposit (diphtheritic dysentery). Ulcers, according to the severity of the case, may be single or multiple. Entire areas of mucous membrane in grave cases may slough; in the milder cases the lesions are more limited.

The *incubation period* of bacillary dysentery is from 2 to 7 days. During this period there are usually no alarming symptoms unless patients have been weakened by previous disease, and if there are no anomalies the second stage is safely reached.

Between the third and fifth days of the disease the character of the *stool* changes. In severe cases the stools are small, bloody; mucus may be mixed with blood; they are less fecal than earlier. Tenesmus and tormina, with the enormous frequency of movements, weaken the patient.

In grave cases there is marked reduction in the quantity of *urine* secreted, albuminuria and casts, and there may be complete suppression.

In the most serious infections the *thirst* is distressing, *muscular exhaustion* extreme, there may be *vomiting* of small amounts *of mucus, intolerant stomach, hiccough* with *sunken abdomen.* Hiccough is not favorable; with subnormal temperature it is ominous.

As a rule the *mind* remains clear even in fatal cases; there are but few *nervous symptoms* save great unrest and inability to sleep because of the *frequent stools and tenesmus.* Frequent small bloody or blood-mucous stools with tenesmus, great thirst, suppression of urine, tormina, small rapid pulse, drawn and pinched expression, sunken eyes, cyanosis, subnormal temperature, cold extremities, include the leading features of the most serious dysenteries. *Temperature* does not offer data for prognosis; in serious cases there may be subnormal or normal temperature while slight rise is of no value. Favorable cases may show several degrees of fever. Bacillary dysentery requires from 2 to 4 weeks before convalescence is reached.

Children, the aged, the feeble, the underfed, and the *dissipated,* offer

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less resistance to bacillary dysentery than do the *active* during mature years, and those who have a good resistance.

The *tendency of bacillary dysentery* is to recover. Convalescence is slow, and relapse promptly follows errors of diet. *Relapses* may last several weeks and merge into *chronicity.*

Gangrenous dysenteric colitis is a grave complication and with symptoms of sepsis, albuminuria or suppression, extreme exhaustion or collapse leads to death in most cases.

Bacillary dysentery is less likely to produce the numerous irregularly shaped and undermining ulcerations, the deep submucous invasion so characteristic of the amebic type. The *prognosis* is naturally more favorable in bacillary dysentery after the disappearance of acute symptoms than in the amebic form, because of fewer complications, more particularly the absence of *suppurative hepatitis.*

Complications

The dreaded abscess of the liver is not a complication of bacillary dysentery. Buchanan reports 1,130 cases with but one abscess of the liver, and Hassler and Morgenroth assert that if present the abscesses are multiple, unquestionably septic metastases. (Coli bacilli and streptococci were found in the pus.)

We had no experience with liver abscess in connection with the epidemics of dysentery in New York State. So far as we know we have met but one case of abscess of the liver following dysentery and that came from the south and was clearly amebic.

Rheumatic pains and **joint swellings** follow or are associated with acute dysentery in about 3 to 5 per cent of all cases These yield to treatment without leaving any permanent disability in most cases.

An occasional complication referable to the heart may prolong the period of convalescence; these are very largely **cardiac neuroses.**

Endocarditis, valvular defects and **myocardial weakness** have in isolated cases influenced the progress of patients.

Bradycardia and **tachycardia** may persist during several weeks, but usually yield without recurring if the patient rests sufficiently. Those who have had the largest experience with dysentery report an occasional neuritis, paraplegia, hemiplegia, monoplegia, paralysis of a single group of muscles, in occasional cases a prolonged period of neurasthenia.

The **peripheral neuritides** offer a favorable prognosis; the outcome of the other paralyses must depend upon the underlying cause. **Neurasthenia** yields slowly to treatment.

Suppurative parotitis is a complication of the graver form of dysentery as is also **empyema**; both complications add to the dangers of an already alarming infection.

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Chronic nephritis occasionally follows acute dysentery.

Chronic bacillary dysentery follows only in a small proportion of acute bacillary infections. Following the cases which developed during the Civil War there were a larger number of so-called "chronic diarrheas." Some of these were mild and easily controlled by diet, some were less tractable, and many veterans are still living who developed the *opium habit* from the taking of the "black drop" to control their symptoms. These patients may live for years and die of the disease, or after long periods of drain they die of exhaustion.

As with most epidemic diseases the *severity of dysentery epidemics* is variable. The Shiga-Kruse strain causes more severe symptoms than do the Flexner or Y bacilli. The first mentioned strain seems to cause more profound constitutional disturbances than either of the other two—the prostration is greater and the number of movements more frequent; hence the mortality is also larger with Shiga infection.

Jochmann claims that with Shiga-Kruse infection the *death rate* is 10 to 15 per cent, with the other strains from 0 to .5 per cent.

Sporadic cases as met in hospital and private practice in the United States offer a good prognosis.

Reference

See Amebic Dysentery.

XIII. Malta Fever

(Undulant Fever, Mediterranean Fever, Neapolitan Fever)

Etiology

Malta fever is a specific infection closely resembling septicemia, due to the Micrococcus melitensis of Bruce (1886) which rages on the islands of the Mediterranean and along its coast; it is characterized by undulatory febrile relapses, excessive sweating, symptoms of arthritis, marked rheumatic pains and enlarged spleen. The disease has at various times been found in Texas. The disease is now known to be due to the drinking of *uncooked goat milk* which is charged with the organism of Bruce. The tendency of the disease is toward chronicity or a subacute course, the average duration being 120 days. There are occasional malignant infections in which the disease runs a rapid course to a fatal termination; these at present are exceedingly rare. The statistics of the Malta garrison show 2,229 cases, with a mortality of 77.

The discovery of the cause has reduced the number of cases, so that its occurrence is now comparatively rare; boiling the infected milk prevents the spread of the disease. The *period of incubation* is from 6 to 10 days.

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The *diagnosis is easily corroborated* by modern blood cultural methods and characteristic agglutination.

Symptoms

The fully developed picture of the disease resembles the *typhoid condition* very closely; in severe cases the *heart muscle* shows weakness, *pulse* may be small and intermittent, there may be *edema of the lungs; pneumonia* is an occasional complication. The *temperature* which follows a short period of malaise may mount to 105° F., but after a few days there is decided remission, evident improvement of all symptoms, after which evening exacerbations become persistent with progressive anemia, malaise, asthenia and enlarged tender spleen. Basset Smith called attention to the reduction of the leukocytes and their phagocytic power.

There is painful *swelling of the joints* and often *swelling of the testes.* Patients grow progressively weaker during these periods which continue 2 or 3 weeks and which are followed by profuse sweating, but they bear the depression well; they then fall into an *afebrile period* which is soon followed by *evening rise of temperature,* and may continue with characteristic *zigzagging of the curve* during long periods.

Prognosis

Bruce contends that one attack produces *immunity.* Manson and Basset-Smith deny this contention.

The *tendency is toward recovery.* The *mortality* is not above 2 per cent.

In exceptional cases early heart weakness may cause collapse and death; there is no stage of the disease which may not be complicated by sudden cardiac asthenia, edema of the lungs, or pneumonia.

The *agglutinating power of the blood* is of great prognostic significance. Values above 1 to 300 are favorable; decided fall indicates early relapse.

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XIV. Asiatic Cholera

(*Cholera asiatica*)

History

Asiatic cholera is an epidemic disease due to the comma bacillus (Koch 1883), and is always spread by an *infected water supply.* The disease was first authentically described by Jessor in 1817, who probably

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observed it during the preceding year in Bengal; it has been *endemic* and *epidemic* for ages in India, the delta of the Ganges never being entirely free. Tscharaka, the Esculapius of India, and his pupil Sucrata who lived long before Christ and recorded their observations in northwestern India, gave a classic description of the disease. The first large outbreak of the disease on the European continent was early in the nineteenth century.

There have been six large cycles of the disease recorded in modern medical literature:

I. 1817 to 1823 in Asia and Africa.
II. 1826 to 1837 in Asia, Africa, Europe, and America.
III. 1846 to 1862 in Asia, Africa, Europe, and America.
IV. 1864 to 1875 in Asia, Africa, Europe, and America.
V. 1883 to 1896 in Asia, Africa, Europe.
VI. 1902—mild—Asia and Africa only

As can be seen from the foregoing data, the United States has suffered several times, and its last experience with the disease was in 1893 when it was brought to the port of New York on several transatlantic steamers; but owing to the perspicacity of the health authorities with the concerted action of an intelligent and well organized profession, it failed to gain a foothold on American soil.

Symptoms

Infection of the *alimentary canal of animals* can be produced by neutralizing the gastric juice with sodium carbonate and the use of opium to prevent intestinal peristalsis.

The disease presents severe *symptoms* of gastro-intestinal disturbance, watery discharges, associated weakness due to depletion and endotoxemia, with, in the severe cases, suppression of urine and other secretions, shrinking of tissues, great prostration, collapse and other symptoms resembling acute arsenical poisoning.

The *blood* in the severe cases becomes viscid because of the sudden and great loss of serum, while in severe cases the specific gravity may reach 1,070 or higher.

In considering the *prophylaxis* and *prognosis of cholera* it is unsafe to ignore the influence of the *carriers* of comma bacilli in producing the disease.

There is a surprising difference in the *virulence of comma bacilli;* hence during an epidemic, rapidly fatal, serious and mild cases may be found at the same time and bacilli may be present in the intestines of *normal individuals,* without causing symptoms. Cholera causes greatest havoc in districts where *sanitation* is faulty and masses are crowded together under unfavorable conditions.

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In offering a prognosis *three stages* must be considered:

1. The stage of diarrhea
2. The cold or algid stage
3. The stage of reaction

1. The Stage of Diarrhea.—Diarrhea may begin toward the end of incubation in some cases in which patients previously had gastro-intestinal disturbances, but usually during the period of invasion. This stage may continue from a few hours (12) to 2 days.

In *severe cases* the movements are frequent, large and watery, associated with marked muscular enfeeblement, small thready pulse, and at once the evidences of depletion with evident loss of weight, pinched facial appearance, pointed prominent nose, sunken eyes, dry skin, great thirst and reduced secretion of urine. The persistent vomiting with these symptoms adds to the danger. There is no way of stimulating or nourishing the patient except through the skin—the large intestine is also intolerant. The pulse grows weaker and smaller; there is feeble systolic force with decided fall of blood pressure to 60 to 70 mm., mercury. At times there is *delirium*. During this stage, however, the mind may remain clear, and death is likely to result.

In the *more favorable cases* the stools become less frequent, the vomiting is more easily controlled, and the urine secretion is increased. *Cyanosis, cold extremities, rapid pulse and sudden urinary suppression,* usually lead to death.

Decided fall of temperature (3 to 5°F.) with any of the above mentioned alarming symptoms during the first stage is dangerous.

The *dryness of the tongue and throat* which leads to the *vox cholerica* is not necessarily of grave import; though present in serious cases.

The small amount of *albuminous urine* in the more serious cases is loaded with hyalin and granular casts. In this and all stages of the disease, the urine offers valuable indications for prognosis.

The *prognosis is good, in proportion to the ability of the kidneys to withstand the ravages of the disease; hence the quantity of urine secreted becomes a paramount factor in prognosis.*

2. The Cold or Algid Stage.—If the prognosis is grave, the patient grows worse, urine scant, albuminous, or entirely suppressed; the appearance is cadaverous; the stools continue watery, large and frequent; the body is cold; the skin is greyish-colored, in most severe cases cyanosed; the eyes sunken, uncovered and fixed; the pulse small and scarcely perceptible; coma is deep; almost complete analgesia exists; death usually ends the scene between the second and fifth day.

If the case is likely to terminate favorably, the patient slowly brightens; the temperature gradually rises from the low mark to which it fell; the pulse is fuller and perceptible; and the urinary secretion—the import-

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ant factor—is increased, clears itself; and the tongue is moister; the stools less frequent; and vomiting is relieved.

In cases with a severe first stage, the patients often die early in the algid stage.

The *cramping of muscles* is a painful and weakening symptom in many cases.

With nephritis uremia is supposed to be a cause of many symptoms, including convulsions, also a serious complication.

Relapses in cases progressing favorably are not infrequent; this is often true where dietetic errors have been made.

Cholerine, a mild form of the disease, may develop from a *preceding diarrhea;* the symptoms may include many of the more severe forms of the disease, but the prognosis is usually good. These cases are recognized by their more benign course, less collapse, though they may show cardiac weakness, marked renal invasion with less albumin loss than in the severe cholera. Occasional cases of cholerine may develop true Asiatic cholera. In the Hamburg epidemic this proved to be true in 50 per cent of cases. Cholerine is also caused by comma infection.

3. The Stage of Reaction.—In occasional cases *sudden death* early in the third stage follows a severe case which may have improved slightly in the algid stage.

Great weakness and apathy with cyanosis and cold extremities are unfavorable.

Fall of temperature after rise in the second stage, early in the period of reaction with the symptoms above mentioned, is unfavorable.

Patients falling into a *typhoid condition* with elevation of temperature, without marked coma, abundant urinary secretion, and sufficient heart strength to give a fair systolic contraction, offer a more favorable prognosis than do those with the symptoms mentioned in the two preceding paragraphs.

Convalescence may begin suddenly with the appearance of an erythematous eruption and febrile movement.

Coma in the third stage of the disease is always unfavorable and likely to be due to uremia and endotoxemia.

The Blood Picture.—Enormous relative increase of red blood corpuscles is unfavorable; this may reach one to two millions per c. mm. (polycythemia). *Leukocytes* are markedly increased in unfavorable cases—50,000 and over (Biernatzki).

In unfavorable cases the *alkalinity of the blood* is reduced because of the loss of sodium.

The height of the *specific gravity* is of some prognostic value.

Patients infected toward the end of epidemics usually develop *anomalous types of cholera,* but in all of these the prognosis is relatively good.

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Complications

Complications are always of serious moment.

Among the complications are **gangrene, croupous pneumonia**—rarely the catarrhal form—**hypostatic congestion** and **edema of the lungs, parotitis, intestinal ulceration, diphtheritic infection of the intestines, uterus, bladder and vagina.**

Abortion which causes prompt death of the fetus offers an unfavorable prognosis for the mother.

Secondary enteritis—chronic catarrh—may follow recovery from the acute symptoms.

Following recovery, there are as a rule no permanent kidney lesions.

The following general conclusions may be accepted in connection with the data already offered:

Conclusions

Cholera infection without outspoken symptoms offers a favorable prognosis. These patients are, however, subject to the sudden development of severe symptoms on slight cause.

Patients *between* 6 *and* 25 have the best chance for restoration to health.

Individual resistance as an important factor in prognosis.

Fever at any stage of the disease is more favorable than subnormal temperature.

Brightening of the intellect with a good skin reaction, and erythematous eruption is favorable.

Past experiences justify placing the *mortality* of epidemics between 30 and 80 per cent.

Alcoholics offer a grave prognosis.

The *period of immunity* produced by the disease is exceptionally short.

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XV. Plague

(Bubonic Plague, Pest)

Plague is an epidemic disease due to the Bacillus pestis (1894, Yersin and Kitasato), a non-motile, Gram-negative microörganism showing well marked polar staining which may cause either

1. Bubonic plague
2. Septicemic plague
3. Pneumonic plague
4. Pestis minor

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History

Plague has been known since the third century of the Christian era; there are references in medical history which create a strong suspicion that the disease raged before that time, but information is not authentic. The Orient was the original home of the plague, which, during the centuries has invaded the continent of Europe repeatedly and has claimed thousands of victims.

The plague which visited Europe during the reign of Justinian in the second half of the sixth century was unquestionably due to the same infection which caused the plague of Milan in the seventeenth century, which has been graphically discussed and illustrated by Fletcher, proving ignorance of the cause of the disease, save as Pare positively declared that an invisible agent produced it, thus foreshadowing its bacterial origin.

The "Black Death" of the fourteenth century invaded all of the then known world, destroying twenty-five million souls, and it is held by Hecker that one-quarter of the earth's population fell victims to the disease. During the fifteenth and sixteenth centuries bubonic plague never entirely disappeared from the continent of Europe—there were epidemics of varying severity. With the end of the seventeenth century the disease limited its ravages on the continent to Southeastern Europe until 1878 to 1879, when Astrakhan (Russia) was infested. During the early nineteenth century Europe continued free from plague. The epidemics of Hong Kong (1894), Bombay (1896), and Manchuria (1910 to 1911) include our latest experiences with the disease. It spread to many countries, including the West Indies and the United States; San Francisco and California suffered most. The virulence of plague is demonstrated by the experience of Toulon in 1721 when of its 26,000 inhabitants 20,000 were stricken and 16,000 died.

Infected *rats and rabbits* introduce the disease indirectly through fleas which serve to inoculate man by their bites. Fifty per cent of the rat fleas belong to the variety *pulex cheopis,* which rarely bite man—hence the comparative immunity of the human race; neither does the *ceratophyllus fasciatus* bite man freely. "The common brown rat is not a house resident to any extent, so that conditions in England are not very favorable for epidemic prevalence" (Osler). The same is true of the United States and of a large part of the European Continent. In the United States and England we have no conception of the terrors of plague without recalling the frightful mortality of the disease in India where in 5 years there have been, in three provinces almost 5½ million deaths attributable to the disease. In the remaining provinces of India, numbering 200 million souls, there have been 2 million deaths (Osler). At present, plague is endemic along the slopes of the Himalayas, in Bombay and its surroundings, in East African Uganda and the southeast of Russia.

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Mode of Entry

It is easy to understand how the unfortunate barber of Milan conveyed the disease from person to person by his infected unguent, which must have carried the pus directly from the ulcers; for it requires only a slight abrasion or microscopic break of the skin to furnish the point of entry for the bacillus—possibly friction alone is sufficient. The lymphatics promptly transmit the infection and the destructive effect follows.

The bacillus may also be inhaled through the respiratory organs and provoke pneumonia. Whether through the lymphatics to the blood-stream or the lung, the blood is soon surcharged and a condition of profound and fatal sepsis develops. It is well to remember for *prophylactic purposes* that *pus, urine, feces and the expectoration,* may all hold pest bacilli, also clothing and dishes, and that they thrive during long periods in damp and moderately warm surroundings. *Abundant sunlight* and weak (1 to 2 per cent) *solutions of bichlorid of mercury* promptly destroy the offender. Therefore unfavorable surroundings invite the disease.

1. Bubonic Plague

After a *period of incubation* of about 10 days, severe symptoms become continuous after a violent chill and high fever.

The *local manifestations of infection of the skin* are redness, swelling, painful enlargement of the surrounding lymphatics, inflammatory reaction in the surrounding tissues, evidences of mixed infection, suppuration and free discharge of pus.

Infection to surrounding lymphatics is prompt with furunculosis, characteristic carbuncles with central necrosis, and often extensive gangrene. The more favorable cases suppurate, without necrosis or gangrene. The presence of a necrotic or gangrenous center is always ominous.

So-called "plague spots" are of hemorrhagic nature, and are associated with other evidences of purpura. Hemorrhages from the mucous membranes occur (*black death,* including hematuria) and are among the most unfavorable of all cases.

The *development of sepsis* is associated with bacteremia; the bacillus is found in the blood; there is diarrhea, albuminuria, high fever of remittent character, delirium—often wild and uncontrollable—(*pestis siderans*) leading to prompt death in from 70 to 80 per cent of bubonic cases.

In Egypt Gottschlich found (1899 to 1902) that there was a decided *difference in the character of the epidemics* during the winter and summer months. He found that during the summer the disease was widespread over entire villages and almost without exception bubonic, in which the infection spread from rats, while during the winter the pneumonic type was in the ascendency. The infection was "from man to man provoked by

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the massing of the victims in narrowed quarters." The *ravages of bubonic plague* are naturally *reduced* as the diseased rats are exterminated by disease or by man.

To prevent the spread of all types of plague must of necessity include early diagnosis, prompt quarantine, destruction of infected rats and mice, care of the cadaver, proper screening and the use of all modern methods in the care of the sick and the protection of those exposed, including the immunization with the sera—now easily obtained either from the Pasteur Institute (Roux and Dujardin-Beaumetz) or the Institute at Berne (Lustig and Markl). Unfortunately the *period of immunization* is short (3 to 4 weeks).

Haffkin and Gaffky have done yeoman's service in this field and both agree that the *use of the sera* is of enormous value in reducing the mortality of plague. Haffkin believes that the death rate among the injected is "four times less than those unprotected." Gaffky, who represented the German Pest Commission, unreservedly recommends the use of the Haffkin protective vaccination.

2. *Septicemic Plague*

Septicemic plague runs a rapid course with marked hyperpyrexia, deep involvement of the nervous system, delirium, coma, rapidly developing heart weakness (myocardial degeneration); often patients are suddenly overpowered and may die within a few hours or during the first day (*pestis siderans*). When there are purpuric symptoms (with hemorrhages from mucous surfaces), death usually promptly follows.

3. *Pneumonic Plague*

Pneumonia may lead to death without external evidences of lymphatic invasion. In many of these cases the *bronchial glands* show characteristic infection. Thorough search often reveals glandular swellings in distant parts of the body. The *blood* is infected and shows the presence of the bacillus.

Pneumonic plague may be secondary to the clearly established bubonic picture, or the involvement of the lung follows a *severe chill without a prodromal period.* The *evidences of grave toxemia* are fever, headache, vomiting, with or without delirium.

There may be either *characteristic pneumonic sputum or hemoptysis.* The latter with the hemorrhagic cases is always most ominous, for *pulmonary edema* is likely to be present.

The *unfavorable features which are usually present,* besides the symptoms mentioned, are hurried respiration, marked dyspnea, cyanosis and often besides evidences of vasomotor paralysis, marked degeneration of the *myocardium.*

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The pneumonic process may be either *catarrhal* (*bronchopneumonic*) or *croupous.*

The *prognosis of primary pneumonic plague* is uniformly unfavorable, death ending the scene in from 2 to 5 days—as a rule on the third day.

Secondary bronchopneumonia offers but slight encouragement for prognosis; an occasional case has been saved.

4. Pestis Minor

These mild, almost symptomless cases are found at the end of epidemics or during periods when there is a lull. Patients are only slightly indisposed; there may be some tenderness and little swelling of the lymphatics, but insignificant febrile movement and recovery is prompt.

General Considerations

As we have already stated, the heart muscle is the point of attack which yields and promptly ends the life of the plague victims. There are prompt *degenerative changes in the myocardium* and the *vasomotor paralysis* which always accompanies profound toxic states.

Dicrotism is usually present, *blood-pressure reduced,* the heart action enormously accelerated.

Rapid pulse (tachycardia) with characteristic toxemia, final *sudden fall of the pulse* to 80 to 90 often precedes death.

Fall of temperature with *persistence of rapid heart action* is unfavorable. Arhythmia is less frequent than the pulsus paradoxus which is often present with pneumonic plague.

If an occasional pneumonic recovers, there may be (as is often found with ordinary pneumococcus infection) during a considerable period, either *persistent tachycardia,* or what is often found in cases which demanded long stimulation, *intermission and bradycardia.*

The *spleen* is usually slightly enlarged but offers no prognostic data, neither does the *tongue* which is uniformly dry, brown and coated. *Nephritis* is an accompaniment of the severe cases—hence is frequent.

The *blood* shows moderate leukocytosis, and in the majority of cases, the presence of the Bacillus pestis. *The greater the blood infection the more virulent is the disease.* Reduction in the number of bacilli in the blood, and their disappearance is always of favorable significance.

Jochmann, whom I have consulted liberally in the preparation of this chapter, places the *average duration of plague* between 6 and 8 days and the *average mortality* as 70 to 90 per cent. As already stated *pneumonic and septicemic plague offer the most unfavorable prognoses.* The *most dangerous cases* to their surroundings, according to Jochmann, are those of the pneumonic type, in which the sputum and microscopic droplets

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exhaled hold the bacilli, and as they are released, spread the infection, either directly to the lung or to the tonsils, from which, through the lymphatics, the lungs and distant organs are invaded.

Complicating meningitis is uniformly fatal.

The prognosis is always more unfavorable during the *early days* of an epidemic than later.

Alcoholism, chronic metabolic faults, previously existing and depressing infections, all influence plague unfavorably.

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XVI. Tetanus

(*Lockjaw*)

The Infection

Tetanus is a disease caused by the tetanus bacillus (Nicolaier and Kitasato), anaerobic, Gram-positive with one swollen end holding a spore, characterized by recurring spasms, always painful, stiffness of the neck and jaw muscles, with final rigidity of the muscles of the trunk and extremities. When fully developed there is *marked opisthotonos* in most cases, the body may be inclined forward (*emprosthotonos*) or to one side (*pleurosthotonos*). In some cases at times during the course of the disease the limbs may continue extended straight and stiff.

The spore of the tetanus bacillus is resistent to external influence, which accounts for the persistence of the germ in earth and manure during unlimited periods, from which, through wounds, it enters the skin. The bacillus remains localized, and under favorable conditions sporulation follows. The *toxin* produced by the bacilli finds its way into the circulation, is promptly appropriated by the peripheral nerves, and through these is passed to the central nervous system (Meyer). The toxin acts as an *excitant* to the ganglionic motor cells of the cord; hence the *spasms* and *tetanic state of the muscles,* characteristic of the disease.

Tetanus may be conveyed through any objects (such as slivers, utensils, fireworks) which hold the spores.

Puerperal tetanus, tetanus or trismus neonatorum and tetanus rheumaticus, are all due to the same microörganism.

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Tetanus is a widely spread disease over the temperate zones of the earth, but is by no means frequent. In the last consecutive 6,000 cases of internal disease we failed to find a single case of lockjaw. Surgeons report increasing fatalities following burns and injuries from firecrackers and fireworks, many of which are manufactured in buildings where they are easily contaminated.

Factors Influencing Prognosis

There are a number of facts closely related to the *life history of the germ* which materially influence the course and prognosis of the disease. The *virulence of the bacillus* is naturally an important factor.

The shorter the period of incubation, the more virulent is the bacillus and the less favorable the prognosis. There are cases, usually foudroyant, in which the symptoms follow within 3 or 4 days after injury.

With the less virulent bacilli the period of incubation is long, varying from 2 to 4 weeks, and in these cases the picture of the disease is likely to be benign *and the prognosis is correspondingly better.* This statement ought not to lead the clinician to the conclusion that tetanus is ever a disease without danger.

The prognosis is always unfavorable in those cases in which the entire symptom complex of the disease develops suddenly or rapidly after the initial rigidity. Such cases may show the gravest conditions within a few hours, during which there have been repeated tetanic convulsions at short intervals.

In the less serious cases the development of symptoms may occupy a number of days, and *the convulsions are infrequent.* The patient gathers strength to resist the painful convulsions during the longer intervals and in favorable cases gets a fair amount of sleep.

The *frequency of the spasms* is in direct proportion to the gravity of the disease. In the more serious cases the spasms may recur several times during a single hour. In the milder cases an entire day may pass with but one or two attacks.

In the more serious cases spasms are provoked by the slightest touch or movement of the body and in these, *death may suddenly follow during respiratory spasm.*

Persistent sleeplessness with frequently recurring spasms is always grave.

Foudroyant cases may end in from 1 to 3 days. In these, the spasms are frequent, the pain severe, the pulse rapid and small, respirations hurried (20 to 80), and before death there is hyperpyrexia, the temperature reaching as high as 106° to 107° F. The urine is retained and likely to be albuminous. With hyperpyrexia the patient may fall into a comatose state.

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Retention of urine is frequent and is not of itself to be interpreted as a serious symptom.

The *pulse is rapid in serious, but little accelerated in mild cases.*

Sudden tachycardia which persists during one or more hours with *frequent spasms* almost always presages an early death.

Cyanosis is always unfavorable.

The temperature is not materially elevated and offers nothing of value for prognosis, save in those foudroyant cases already mentioned, and in some cases before death it suddenly rises to 105°-107° F. when the patient is likely to fall into coma. With hyperpyrexia there is marked myocardial insufficiency and cyanosis before the end.

The *wound itself* offers nothing which serves to guide the clinician in offering a forecast of the disease.

If at the height of the disease there is a *decided increase in the frequency of the tetanic spasms* the prognosis is bad.

In favorable cases improvement includes the lengthening of the interval between the attacks, decrease of muscular rigidity and pain, ability to swallow without spasm, improvement of the pulse, return of the temperature to normal, and decided change in the facies of the patient.

Before a favorable prognosis is justified in any case of tetanus all symptoms must continue favorable during several days, for relapse cannot be excluded until convalescence has been fully and permanently established.

The duration of the disease is variable; death may follow only a few hours or a few days (2 to 6) or there may be from 6 to 10 weeks of uncertainty. The long drawn out cases usually recover.

Convalescence is usually prompt, and it is surprising to note how rapidly, as a rule, the patient regains his health and strength without sequelae.

Myocardial weakness may persist during several weeks with some cardiac dilatation. Full recovery from this sequel is the rule as well as from arhythmia, which occasionally follows the acute period.

Puerperal tetanus may develop in from 3 to 15 days after confinement, is fortunately rare, but almost always leads to death.

Trismus neonatorum usually develops from 4 to 10 days after birth and is almost uniformly fatal. There are cases on record which were also fatal in which the periods of incubation of both puerperal tetanus and that of the newborn were as long as 3 weeks.

The *mortality of tetanus* is high in cases untreated by modern methods. Of the cases with a short period of incubation, less than 10 days, Rose reported 96.7 per cent of deaths, against an average mortality of 80 to 90 per cent.

The prognosis of tetanus is unquestionably favorably influenced by the *routine use of prophylactic injections of the tetanus antitoxin* after

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injuries. Already there are sufficient evidences at hand to justify the foregoing unqualified statement. So far as the influence of tetanus antitoxin on the course of the disease after its full development is concerned, we have few favorable results to offer.

There are a number of cases recorded in medical literature in which the *injections of magnesium sulphate* (intraspinous) after the method of Meltzer, with the free use of the tetanus antitoxin have been followed by recovery. There are also cases in which the hypodermic use of magnesium sulphate has seemed to influence the spasms favorably (Meltzer).

Kocher found the prognosis bad and the magnesium sulphate contraindicated when the cerebrospinal fluid failed to flow.

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XVII. Anthrax

(Woolsorters' Disease, Malignant Pustule, Milzbrand)

The Infection

Anthrax is a disease of sheep and cattle, caused by the Bacillus anthracis, a large, Gram-positive bacillus, which spores outside the body and is conveyed to man either through the skin directly, the lungs, or the alimentary canal, occasionally through the nose and mouth. Pollender in 1855, and Brauell in 1857, described the bacilli now known to cause the disease after a period of incubation averaging 7 days. The most frequent *source of the infection* in man is through the skin from hides, wool and pelts of the infected animals; there are some who contend that insects through their sting may also convey the disease from infected animals to man.

Anthrax may be either (1) external or (2) internal, and is classified as follows:

1. External anthrax.
   (a) Malignant pustule.
   (b) Malignant anthrax edema.

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2. Internal anthrax.
   (a) Gastro-intestinal (alimentary mycosis intestinalis)
   (b) Respiratory.
   (c) Splenic.

External Anthrax

(a) **Malignant Pustule.**—Malignant pustule is the most frequent variety of anthrax found in man. Its early recognition and rational surgical and serum treatment save many patients. The fact that with anthrax there is less pain than with the ordinary furuncle, leads to delay in treatment and to consequent serious constitutional invasion. Rapid extension of the pustule with spreading and deep central gangrene, hemorrhagic vesicles in the periphery, extensive infiltration, erysipelatous blush with marked constitutional symptoms, are *evidences of malignancy* and demand a guarded prognosis. Marked lymphatic extension and tenderness with glandular enlargements are not always of serious moment; their improvement without increase of constitutional manifestations after radical treatment is always encouraging.

If the pustule is neglected, the prognosis is accordingly influenced unfavorably, for before the end of the first week there are symptoms of sepsis, including fever, delirium, diarrhea, vomiting, hematemesis, foul coated tongue, anorexia, enormous prostration, wasting, enlarged spleen, and after a period of collapse in many cases with myocardial weakness and continuation of the septic symptoms for from 2 to 4 days, death ends the scene.

There are *foudroyant cases* in which evidences of sepsis are early and the development of grave symptoms is rapid in which death may follow within 2 days after the appearance of the skin lesion.

Two-thirds of skin infections recover.

(b) **Malignant Anthrax Edema.**—This variety of external anthrax is fortunately less frequent than is the malignant pustule. It is more frequently found with invasion of the face, i. e., eyelids, head, hands or arm. The *pustule is absent,* but the edema is rapidly formed and is diffuse. Sepsis is promptly developed and is severe; heart weakness and deep invasion of the nervous system are at once alarming. The prognosis of the edematous variety of external anthrax is *almost uniformly fatal.*

2. Internal Anthrax

The diagnosis of all types of internal anthrax is exceedingly difficult and in most cases impossible, as a rule it is made post mortem only.

(a) **Gastro-intestinal Anthrax** (*Mycosis Intestinalis*).—The prognosis is almost uniformly bad. There are early evidences of grave infec-

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tion with symptoms of severe gastritis, including vomiting, often hematemesis, bloody diarrhea, prompt evidences of sepsis, including fever and weak heart, tympany and abdominal tenderness with other symptoms of peritonitis and enlargement of the spleen. In some of these cases there are evidences of cutaneous malignant purpura with bloody vesicles. Cases of alimentary anthrax rarely live beyond the third day of the disease. The mortality varies between 50 and 87 per cent. (The *post mortem appearances* are characteristic and show changes in the mucosa of the stomach and intestines, including elevations varying in number (20 to 50) with central necrobiotic patches, black sloughs and consequent ulcerations, besides the enlarged spleen already mentioned.)

(b) **Respiratory Anthrax.**—There are occasional cases of respiratory anthrax which show less tendency to pulmonary edema than does the malignant type, which run a subacute course varying from 2 to 5 weeks, ending in recovery. These cases are exceptional.

The *majority of pulmonary invasions offer but scant hope of recovery.* The *mortality* may be as high as 50 to 90 per cent. They begin with many of the symptoms of a severe pneumonia, promptly develop pulmonary edema, and the victim drowns in his own serum. Pleurisy is frequent. There is in the severe cases a violent *initial chill* with *high fever,* and early manifestations of *cardiac toxemia.* The *extensive transudate into the alveoli* causes distressing dyspnea, cyanosis, and evidences of carbonic acid poisoning. In these malignant cases, the sputum is promptly bloody after a short period during which it may be serous. *Hemoptysis* is not infrequent within the first 24 hours, or it may precede death on the second or third day of the disease. The heart is rapid from the beginning and soon shows the strain due to *toxemia* and possible *secondary pulmonary obstruction* (edema, etc.). *Diarrhea, delirium* and *coma* are always alarming symptoms.

Infection of the nasal passages, larynx, treachea or larger bronchi, with or without pulmonary anthrax, adds an enormous element of danger and usually causes death.

The majority of cases of the respiratory type are found among *ragpickers* or *woolsorters,* and as all other forms of internal anthrax, are usually fatal. Death follows after 2 or 3 days of symptoms from cardiac asthenia or because of the reduced respiratory surface due to infiltration and edema.

(c) **Splenic Anthrax.**—Cases of splenic anthrax run a fatal course without pustule or other evidences of local disturbance, but with all of the symptoms of the more virulent and malignant types of the infection, including brain symptoms due to *embolic infarcts* causing *hemorrhages into the cerebral cortex* and the usual evidences of sepsis, characteristic of all fatal cases.

Encouraging reports which prove the value of the *antianthrax serum*

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are multiplying and justify a more hopeful view of the outcome of those cases of anthrax which are recognized early and which are promptly injected and treated, than has been offered in the past.

Pasteur's prophylactic vaccination of cattle and sheep has reduced the mortality among these in France to one-twelfth the former number, while the production of active immunization by means of the Sobernheim serum, now largely used on the continent of Europe, seems to be more certain and lasting in its effect—all of which argues favorably for the protection of mankind against the disease and the consequent limitation of its ravages.

XVIII. Glanders

(*Farcy, Malleus, Die Rotz*)

The Infection

Glanders is a highly contagious disease, due to the Bacillus Mallei (Loeffler-Schütz Bouchard, 1882), a Gram-negative germ, which after a period of incubation, varying from 3 days to as many weeks (usually from 3 to 4 days) is followed by symptoms of sepsis, suppurating and granulating ulcerations, either of the nose or skin, with a tendency to spread over the body rather than to remain localized.

The tissues around the ulcers are infiltrated. The ulcers are crater-shaped after a period of pustulation when the skin is involved.

The *disease is contracted* from infected horses, mules, donkeys, rarely from other animals; the *secretion of the ulcer* in the nose, occasionally of the skin, *holds the disease-producing bacillus.* Those working in stables and on ranches are oftenest infected. The disease is either: (1) Acute glanders, or (2) Chronic glanders.

1. Acute Glanders

Acute glanders *runs a rapid course to a fatal termination* as a rule in from 7 to 14 days. The serious nature of the infection is recognized by the weakness and wasting during the period of incubation after which *the severe chill, immediate constitutional symptoms and the facies of the patient with local manifestations, promptly prove the presence of grave disease.*

The *spleen* is usually palpable and enlarged.

The *site of infection* shows changes early; there is redness, swelling and great pain when the skin is involved with the development of *vesicles, pustules and ulcers.*

Nasal infection is associated with early symptoms of dry catarrh, soon followed by ulceration and abundant secretion which becomes foul-smelling and purulent. Nodes form on the mucous membrane of the nose, are

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often found on the *conjunctiva, in the mouth, pharynx, larynx, bronchi, lungs, intestines,* and after 7 to 10 days appear in the muscles, usually those of the arm (biceps) the chest and calves.

In occasional and rapidly fatal cases the disease begins with symptoms of *transitory facial erysipelas* or marked redness of the face after which the true nature of the disease is manifested in the development of the nasal and cutaneous changes.

In all cases the *lymphatics* in the neighborhood of the lesion are swollen and tender.

There are *acute and rapidly fatal cases* in which the early symptoms are those of general sepsis, which latter antedate all local manifestations and obscure the diagnosis. There may be periarticular swellings with pus formation and infiltration.

Far-reaching invasion of the lung is uniformly fatal.

The usual changes found with general sepsis in vital organs, *heart and kidney particularly,* increasing weakness of the former, insufficiency of the latter, are prominent before death.

The character of the fever varies, but as a rule, it is intermittent; the sweats are often profuse and weakening, and with a rapid small pulse, such cases die during the second or third week.

The onset of delirium or other symptoms of *deep involvement of the nervous system,* including coma is always ominous, usually fatal.

2. *Chronic Glanders*

This form of the disease may persist during a number of months or several years with exacerbations of all of the symptoms and multiple lesions of the acute cases already considered, including ulcerations, many abscesses, muscle nodes and lymphatic enlargements. Bollinger reports a case which lasted 11 years, while Romberg mentions cases which continued with irregular fever 1 and 2 years.

Recovery from chronic glanders is not exceptional and may follow in 50 per cent of cases. Bristow reported a case which he persistently treated with an *autogenous vaccine* in which the patient made a full recovery.

Prophylactic measures which include the prompt killing of all infected animals and the thorough disinfection of stables, cleanliness and the use of antiseptics by those who are exposed, with the early injection of mallein (a filtrate a dead glycerin and boullion culture of the Bacillus mallei) offer the only methods of controlling the ravages of the disease.

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XIX. Leprosy

(Lepra; Miselsucht (German); Meltzei (German); la Lepre (French); la Lebbra (Italian); Spedalskhed (Norwegian); Melaascheid (Dutch); Elephantiasis graecorum)

The Infection

Leprosy is a chronic infectious disease due to the lepra bacillus of Hansen (1871) (Bacillus lepræ), which has been known for ages, is mentioned in the bible, in the old literature of India, was prevalent among the Egyptians, the ancient Jews and Greeks, many centuries before the Christian era. The history of leprosy includes one of the most interesting and important chapters of medicine, and should be studied by the student, that he may gain an idea of the importance of the infection during all of the ages, the sufferings of its victims, who were always feared, and usually banished to exile, too often neglected. Even Moses banished the afflicted from the camps of the Children of Israel. Since time immemorial the civilized and semi-civilized nations have all treated the leper with the same fear and have left him to his fate. It is a strange fact that in Norway and in Portugal, leprosy has continued endemic to the present day, also in the West India Islands.

With the introduction of syphilis in the fourteenth century leprosy seemed to recede. The disease was introduced into America by the African negro slaves. Indians seem to resist the infection while the European, the mixed races and negroes are most susceptible (Krause).

Leprosy is *not hereditary;* it may be transmitted just as is tuberculosis. The new born babe has not been found infected, and the youngest leper children are not older than from 3 to 5 years. All persons above the third year may be attacked.

Leprosy has a *period of incubation* which may extend over many years (3 to 32). The disease is *rarely conveyed to the attending physician or to the nurses.* For over 25 years we have been interested in the fate of a number of noble Sisters of Charity who went from St. Joseph's Hospital, with which we have been connected, to Molokai in the Sandwich Islands; they have been in close contact with the lepers of the colony and all have continued free from infection.

The disease is characterized by symptoms of three types:

1. Tubercular type.
2. The anesthetic type.
3. Mixed type.

1. The Tubercular Type

This type includes skin changes in which, during varying periods, there are hyperesthetic and reddened macules usually on the face and

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hands, later on the legs (elpra maculosa) in which nodules (tubercles) finally develop which undergo *retrograde change* (*necrobiosis*), *ulcerate,* often involving the underlying tissues including the *tendons,* the *bones* and the *adjacent soft parts.* In some cases there are but few or no tubercles or nodules; the skin continues anesthetic, becomes pigmented, and shows other trophic changes; the spots of original erythema may bleach, becoming strikingly white (lepra alba). Sensory changes may develop very slowly; when once present they persist.

Fever may precede the development of pigmentation or other visible trophic changes (lepra alba).

The *hair* is usually diseased or lost; *mucous membranes* may show marked changes (including the conjunctiva and nasal mucosa); ulcerative keratitis and deep *ocular changes* may lead to far-reaching destruction and blindness.

Many lepers of the tubercular type die of laryngeal invasion or pneumonia. The prognosis is absolutely bad. The tubercular type of leprosy is more contagious than is the anesthetic. The nasal secretion according to Sticker holds the infecting bacillus, and he believes that the disease is spread from this course. Meier has proved that 70 *per cent of tuberculous lepers offer a positive Wassermann reaction.*

Sexual intercourse is not an important factor in transmitting the disease; its influence is greater when the victims live under unsanitary conditions. Munch found that with marriage of short duration of a leper and non-leper, the disease was transmitted in 2.5 per cent of cases; while with those who lived together in matrimony during long periods of time the statistics showed 11 per cent of transmissions.

Early invasion of the mucous membranes particularly the larynx is unfavorable so far as the duration of the disease is concerned.

2. *The Anesthetic Type*

The anesthetic type of leprosy is characterized by anesthesias and hyperesthesias. There are severe pains in the extremities (usually the legs) with hyperesthetic areas or there may be anesthesias. In some cases there are both anesthesic and hyperesthetic patches. As the disease develops, the *nodules* may easily be felt along the nerve trunks, and the *trophic changes* are marked. These include the formation of blebs with final ulceration which is deep and extensive, *changes in the extremities,* usually the toes and fingers, in which there are contractures, destruction of tissue and gangrene of terminal phalanges.

The prognosis so far as life is concerned with anesthetic leprosy is not bad, for the patients may live and continue useful during many years; as a rule they die of *intercurrent disease.*

The *deformities* due to loss of tissue and contractures prove a serious handicap, as do the anesthesias and paresthesias.

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3. The Mixed Type

The possibility of the mixing of the two types in the same patient must be remembered. The tubercular type is very likely to develop peripheral anesthesia and the patient dies with "mixed leprosy." The anesthetic type is not likely to develop the characteristic "tubers" of type 1.

Leprosy predisposes to tuberculosis; about 30 per cent of lepers were found tuberculous at the Trinidad Asylum.

Nephritis is a frequent and serious complication; Abraham's statistics showed that 32 per cent of 109 lepers autopsied had kidney disease. "There was no specific leprous invasion" of the kidney.

Death may follow 1 or 2 years of infection in rare cases; there are on the other hand cases in which the disease has appeared to be arrested—even cured—while a period of 40 years has been recorded in some instances. Abrahams reports 18 years as the average duration of cases in Trinidad, 6½ years for the nodular; 10 years for the anesthetic types, and 9¾ years for the "mixed" cases.

In young subjects the disease progresses more rapidly than during the active years of life, this is true of the anesthetic type particularly.

Invasion of the internal organs always shortens life.

With *far-reaching infiltration of the skin* the progress is slower than with multiple tubercle deposit.

The number of cases is being rapidly reduced by the segregation of lepers and their proper hygienic care.

Relapse

The majority of cases which have been watched in which recovery was suspected, relapse after long or short periods, finally running an exceedingly chronic course.

It may be safely assumed that "once a leper, always a leper."

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XX. Tuberculosis

Tuberculosis includes all diseases caused by the Bacillus tuberculosis of Robert Koch (1882), which latter causes the formation of nodular deposits (tubercle), or diffuse infiltrating masses, showing tendency to be-

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come caseated, causing ulceration and breakdown of included tissue, with an effort on the part of nature to heal by the formation of new connective tissue, calcification, the enclosure of deposits and the walling off of cavities. *The disease is infectious, contagious, preventable and curable.*

History

There have been epoch-producing periods and events in the history of tuberculosis which have cleared the horizon, proved the cause and pathology of all tubercular processes, extended our knowledge, made diagnosis positive, established rational methods of treatment and prophylaxis, and have further entirely changed the prognosis of all forms of the disease.

Medical history includes references to tuberculosis, centuries before the Christian Era. Hippocrates understood and described the manifestations of the disease 400 years before Christ; Celsus, Aretaeus, and Galen were also familiar with the disease but added little to the work of Hippocrates. The first advance was made when Sylvius (seventeenth century) *demonstrated the association of nodular deposits with consumption.* He considered these enlarged lymphatic glands. The next advance was made when Morton, a contemporary of Sydenham, in 1689 contributed a work in which he gave a classic description of the *clinical history of the disease.* Morgagni and Baillie followed, *denying the identity of the tubercle nodules and demonstrated that they are not enlarged lymphatic glands.* Their *gross anatomic structure* was recognized. The two most important advances of the early nineteenth century were: (1) the recognition by Bayle of the *anatomic structure of the miliary tubercle* with the recognition of its general distribution, and its importance in causing *constitutional disturbances,* and (2) the establishing by Laennec (himself a victim of the disease) in 1819 of the most valuable of all knowledge connected with tuberculosis, save the discovery of its cause, *the unity of all tuberculous lesions.* At first his dictum was controverted; even Virchow remained unconvinced and differentiated *cheesy pneumonia and other tuberculous processes.* Fortunately Virchow lived long enough to change his views and subscribed willingly to the established conclusions of the French clinician.

Valsalva and Morgagni understood the *contagious nature* of tuberculosis.

It remained for Villemin by experiment in 1865 to offer the next great advance in the history of tuberculosis and *to lay the foundation of all advances* which have followed since his day in connection with this disease. He proved the *communicability and the infectious nature of all forms of tuberculosis,* pointing the way to the search for its cause. Villemin's work has failed to receive the attention and the praise from the profession which its enormous importance deserves. His name will live in history so long

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as our science and art shall endure. Cohnheim, the leading pathologist of Germany, ridiculed the conclusions of Villemin; but he too lived to acknowledge his error and subscribed fully to knowledge which is now universally understood by the professional and lay world.

In 1882 Robert Koch, a quiet, modest, almost unknown observer, working patiently away from the large medical centers, gave the world the results of his investigations and demonstrated the Bacillus tuberculosis as the real cause of all forms of tuberculosis, wherever located.

Then followed in rapid succession the appreciation of the needs of the tuberculous sick by such men as Brehmer in Germany, and our own Trudeau, the underlying basis of their success including the full appreciation of the life history of the infecting agent, the resistance which the patient offered when placed in a favorable environment reinforced by the strength which resulted from pure air, a flood of sunlight on the body and on the germ as well, with the pabulum so much needed to lift the resisting power of the patient to par or above. Alonzo Clark, my revered teacher in 1877 and before, repeatedly insisted that *"tuberculosis can never advance in normal tissue or when the patient's health is at par,"* to which we add to-day: *the tubercle bacillus does not readily proliferate or find a suitable habitat in normal tissue. The germ lies ready to attack, and the disease progresses when vitality is lowered and tissues are changed from the normal.*

The final factors which have influenced the prognosis of tuberculosis have been the *education of the people,* and the *growth of professional knowledge* which makes the early recognition of the disease possible. The tuberculous subject to-day enters upon the early treatment of his condition fully instructed, with hope and the belief that by natural methods he will either be cured or his disease will become latent. The factors previously mentioned have influenced prognosis favorably in all civilized countries during the past 30 years. The data collected by statisticians, particularly those of Hoffman, deserve recognition and wide publication.

In the United States, statistical evidence proves that the *mortality from pulmonary tuberculosis* has actually and relatively diminished; "that on the *basis of rates for the registration area,* the saving of lives due to the campaign against this disease during the decade ending 1910 alone, has amounted to nearly 200,000." The *death rate* during the past decade has been reduced from 174.5 per hundred thousand of population to 139.7. *Hoffman's study* of the combined mortality from tuberculosis of the cities of New York, Philadelphia and Boston for 100 years, commencing with 1812, *shows a persistent reduction of the death rate* from 418.6 per hundred thousand population in the first decade of this period to 213.9 in the last decade. This tabulation of Hoffman's is the first ever made for any group of large cities and establishes the fact that the *greatest reduction commenced with the discovery of the tubercle bacillus in 1882* and the

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education of the masses. The death rate in 1881 was 389.1, in 1912 it had declined to 180.1 per 100,000. A study of 50 large American cities for the 40 year period beginning 1871 shows a fall from 335 per hundred thousand in 1881 to 166 in 1911.

In the northern and western cities the decline was from 325 to 160 per hundred thousand, or 50.8 per cent.

Among the *whites of the southern cities* the fall was from 301 to 150 or 50.2 per cent; the *colored population* showed a reduction from 668 to 423 or 36.7 per cent.

Massachusetts, Rhode Island and Connecticut show a decrease from 276 per 100,000 population in 1881 to 146 in 1911—47.1 per cent.

The reduction in the death rate for women is greater than the decrease for men.

The statistics as collected by Hoffman—a work for which the profession owes this layman an everlasting debt of gratitude—prove that the reduction "in the *tuberculosis death rate in the United States* during the last 40 years has not been less, but in many cases more than in other civilized countries throughout the world."

In England the drop in the death rate during the past 40 years is almost 50 per cent.

In London from 1901 to 1910 (Osler) the death rate from consumption has dropped 33 per cent; all other forms of tuberculosis have been favorably influenced.

In Germany there has been a like and encouraging reduction.

For the clinician, in the light of our present knowledge, it is safest to recognize *two pathogenic types of bacilli as the cause of human tuberculosis:*

I. Typus humanus (Koch).
II. Typus bovinus (Theobald Smith).

The overwhelming number of cases are due to the typus humanus of Koch. A bitter war has been waged in connection with the part played by the bovine tubercle bacillus in causing human tuberculosis. von Behring is a strong advocate of the theory of *bovine tuberculosis,* introduced by milk (*enterogenic infection*) as the main cause of pulmonary tuberculosis, assuming that the bacilli remain latent in the lymphatics during many years; to which Calmette vigorously subscribes. Robert Koch in London at the Congress for Tuberculosis (1902), and often after that memorable occasion, held opposite views. *Koch did not believe that the bovine bacillus was pathogenic for man,* and advanced strong arguments to prove his contentions. The *conclusions of Kossel* are as follows:

1. Pulmonary tuberculosis with few exceptions depends upon infection with the typus humanus.

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2. Tuberculosis is conveyed from man to man by means of the Koch bacillus.

3. Bovine transmissions of tuberculosis to the human subject through milk or meat (typus bovinus) is rare and of minor importance.

It will be noted that Kossel, an ardent disciple of Koch, does not commit himself against the possibility of bovine infection, but concludes that *"to control tuberculosis, contagion from man to man must be prevented."*

Orth contends that 10 per cent of all forms of tuberculosis of early life are of the bovine type and cites Kossel's own statistics to prove the truth of his contentions. These show the *bovine type* in 4.3 per cent of bone tuberculosis, 10.7 per cent of tuberculous meningitis, 23.8 per cent of general tuberculosis, 40 per cent of tuberculosis of the neck glands, and 49 per cent of all forms of abdominal tuberculosis. Orth's conclusion for our purpose is significant: "tuberculosis cannot be effaced so long as bovine tubercle bacilli are conveyed from infected animals to man."

Heredity as a Factor in Prognosis

Does heredity, by the transmission of tuberculosis from parent direct to the offspring, influence prognosis? This question has been vigorously debated during the centuries. We are agreed that both in man and in the calf *congenital tubercle is so rare as to be a curiosity.*

The child is not born with tuberculosis, the disease is acquired. Bandelier and Roepke contend that medical literature includes but 120 cases of congenital tubercle, of which only 20 bear close scrutiny. *Tuberculosis during the first months of life is exceedingly rare.*

I have repeatedly used the *von Pirquet test in babes, the offspring of tuberculous mothers or fathers,* with negative result until the time of infection. One of the great advantages of the *von Pirquet* test for diagnosis and prognosis is the fact that *the time of infection can be established by it.* If in a child, the offspring of a tuberculous parent there are no symptoms and the test is negative, later symptoms develop and another test is positive, it may be concluded that tuberculosis wherever located has not existed long.

What the offspring of the tuberculous parent inherits, is a vulnerability, a predisposition, which makes the child ready to develop tuberculosis on slight cause. The *susceptibility* in other words *is greater in the offspring of the tuberculous than in the child coming into the world without handicap.* Every clinician of experience numbers *"tuberculous families"* among his clients. The following quotation is clear and to the point: "Dr. Horder says that the existence of tuberculous families is one of the cardinal facts in clinical medicine, and I agree with him; but on this point I am disposed to make one or two remarks. I would oppose the too frequent assumption—not by the present writers—that the victims

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of tuberculosis are after all weaklings whose weeding out is painful to their friends, is on the whole, good for the stamina of the race. It is true that by inheritance or by privation, a person may be so debilitated as to offer a lessened resistance to any injurious influence from without; but, on the other hand, in respect of tubercle, such a lack may mark a family from generation to generation, as a peculiarity rather than a frailty, or at worst, as a flaw which is open to one kind of stress only." "Such a constitution is as a lock, which may be shut to every key but one. Bar the tubercle, and such a one may continue strong and beautiful" (Allbutt). Brehmer found that *the youngest children of tuberculous parents and their children in turn were most disposed to tuberculosis.*

Children of the tuberculous show a *higher mortality than do those of non-tuberculous parents,* the death rate decreasing as these children grow older. The death rate is greatest among these children, the nearer their birth to the time of the parents' death. We have found under improved environment that the removal of these children from the danger of infection is a most important factor, for thereby their lives can often be saved.

Congenital stenosis of the pulmonary valve invites tuberculosis. It is the exception to find a child with this defect without tuberculous infection after the fifteenth year; often earlier.

Alcoholics with inherited susceptibility are ready victims.

The *habitus phthisicus* predisposes to pulmonary and other forms of tuberculosis. The misshapen chest, the small heart, the tendency to glandular enlargements (lymphatism) and the habitus asthenicus (Kraus, F.) including faulty growth and development, are among the factors which invite in the vulnerable, the non-resistant, and predisposed, the development of tubercular phthisis.

Acquired and Inviting Factors

Acquired and inviting factors are of paramount importance in the development and progress of tuberculosis.

All diseases which lower vitality increase susceptibility to tuberculosis. Improper diet, bad air, insufficient ventilation, crowded cities, tenements, impurities of all kinds, inhalation of dust, poor clothing, prolonged dampness, sedentary occupations, pernicious habits, alcoholism, worry, want, the crowded prison and workshop, all lower resistance and invite tuberculosis. *All acute and chronic respiratory diseases* which are associated with changes in the *bronchial nodes* or *respiratory mucous membrane,* unless controlled by treatment or placed in favorable general condition, offer a ready culture medium for the tubercle bacillus.

A large number of children are infected from tuberculous invasion of the bronchial lymph nodes which has remained latent during months at times, following measles, whooping cough, pneumonia (lobular and lobar), acute bronchitis, scarlet fever (less often), and other infections.

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In the adult, *typhoid fever, malarial, and influenzal diseases*, as well as *syphilis*, also prepare the individual for further infection by the tubercle bacillus. Usually they kindle a latent process into activity. *Diabetes* and *pregnancy* are among the inviting conditions. When tuberculosis follows *pleurisy*, the latter was in all probability of tuberculous origin also.

There are *diseases which seem to offer resistance to the progress of tuberculosis;* these include gout, nephritis, asthma, emphysema, and mitral stenosis. The consecutive hyperemia associated with mitral stenosis is held to be antagonistic to the development of tuberculosis. The *infection* with tubercle bacilli *of the majority of mankind* at some time during life, usually before the twelfth or fifteenth year, unquestionably produces a degree of *immunity* and proves an important factor in prognosis later in life. *von Behring believes that the favorable course of chronic tuberculosis in the adult is due to this acquired and relative immunity.*

Tuberculosis is *a disease of all ages.* By predilection it chooses the lymph nodes, bones, and the meninges in early life. The importance of *latent tuberculosis* at all ages deserves serious consideration as a factor in the sudden dissemination of acute miliary disease.

The *prognosis* of any form of tuberculosis presents serious difficulties owing to the *variety of anomalies* with which the disease may be associated, *the inherent tendencies of all tuberculous deposit, the inability to measure at any stage of the disease the resistance of the infected individual and the intensity of the infection.*

It is not always possible to estimate the *extent* and *location of the disease.* There is scarcely an organ of the body which may not harbor one or more tuberculous deposits for years without revolt and without subjective or objective symptoms. *Prognosis therefore must rest upon the clinical manifestations of the individual case and their association with such pathologic changes as are made clear by physical examination and the refinements of diagnosis.* No man can safely pierce the future of any form of the disease who has not a thorough understanding of the characteristics of the tubercle, its inherent tendencies including its easy breakdown, ulceration and caseation, the possibility of reparative and protective processes, its frequent latency as well as the enormous variations in the resistance of those infected.

1. Acute Miliary (General) Tuberculosis

Acute general miliary tuberculosis, in contradistinction to acute pulmonary miliary tuberculosis, is a far-reaching general infection, secondary to an existing focus, which is *spread by the blood-stream*, characterized by the formation of *millet-seed-sized tubercles* in large numbers, *in many organs at the same time.* Acute miliary tuberculosis is always proof of initial invasion of either a blood-vessel or lymphatic (thoracic duct), from

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which bacilli are distributed to distant organs (Weigert). Experiences with acute miliary tuberculosis prove the importance of cautious observation of all children and adults who have *periods of indefinite symptoms* in which *positive diagnosis cannot be made* and those who have had other *acute or chronic infections* which are likely to leave *foci which invite tuberculous deposit.* This is true of all acute diseases of the lung and bronchi which may be associated with *latent deposits in lymph nodes,* from which, as the general health of the host is reduced, bacilli find their way into the blood-stream (vein, artery, or lymphatics). There is often direct dissemination through the lymphatic channels from the thoracic duct into the right heart. *Neglected pleurisy* may supply the infection.

Otitis media, the suprarenals, the genito-urinary tract or any of its separate organs, bone, or joints serve in different infections as the *primary focus.*

Infection through the aorta and heart wall, the pulmonary artery, the carotid, may spread *miliary disease.* With miliary as in all forms of tuberculosis the *vulnerability and susceptibility of the carrier* of a latent focus become important prognostic factors. Ribbert called attention to the conservative processes which in the resistant prevents the entrance into and the invasion of the blood. In these there is a strong tendency to prevent contamination by protective local hyperemia, marked dilatation of vessels, acceleration of the local circulation, etc. The depressing and weakening effect of *pregnancy* and *childbirth* become important factors in lowering the resistance of the patient and spreading infection.

There are three clinical forms of acute miliary tuberculosis, each of which is characterized by the presence of leading symptoms:

I. The typhoid form.
II. The pulmonary form.
III. The meningeal form.

I. Typhoid Form

The typhoid form of miliary tuberculosis resembles enteric (typhoid) fever, in so many ways, that but few men of large experience will deny having made errors of diagnosis. There may be and usually is *enlarged spleen, albuminuria and irregular fever,* which may assume the typhoid curve! *Diazo* (Ehrlich) *reaction* is positive; *heart sounds rapid; systolic murmur* distinct in many cases. Unless there is complicating *tuberculous meningitis,* the pulse may be *dicrotic and rapid.* If there is *meningitis,* during its early stage the pulse is slow.

The symptoms which are unfavorable include: *rapid pulse, low blood-pressure, marked apathy, involuntary discharges of urine and feces, and albuminuria.*

Leukopenia and reduced hemaglobin, in some cases, and *relative reduc-*

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tion of lymphocytes have characterized the graver and more acute forms of miliary infection. *Leukocytosis of moderate degree* is occasionally present. *Hurried and irregular respiration* with or without cough, *Cheyne-Stokes breathing*, are all unfavorable and are soon followed by death.

II. Pulmonary Form

With evidences of acute infection, but without the marked and positive physical signs of acute pneumonic tuberculosis, there is a progressive loss of strength, with lung symptoms in the ascendency. These include dry cough, but little or *no expectoration*, at times *rusty sputum*, mucopurulent, rarely *hemoptysis*. It is difficult to make the accurate anatomic localization of lung changes, for the percussion note may not be changed and in many cases there are but few râles. In children the pulmonary form of *acute miliary tuberculosis may promptly follow measles, whooping-cough, typhoid or other infections;* or the *bronchial nodes* infected during these diseases may later, *after long periods of latency*, without symptoms and in apparent health, erode vessels or lymphatics and lead to general and fatal miliary tuberculosis. When any of the forms of miliary tuberculosis follow immediately on the acute infections the prognosis is absolutely bad, progression is rapid. The physical signs depend upon the size of the deposit, the amount of bronchitis and the associated acute and chronic changes. In some cases there are evidences of *old and latent disease*, there may be general infection with all of the symptoms of sepsis and no evident change in *old deposits* long recognized, which are the direct cause of miliary dissemination.

With associated *broncho-pneumonia* the lung symptoms are most prominent. I have seen both lungs studded with miliary tuberculosis at the autopsy in cases which presented no positive physical signs during life. In such cases *x-ray examinations* will strengthen diagnosis and prognosis.

The pulmonary form of acute miliary tuberculosis may be associated with the *typhoid condition* and to this may be superadded tuberculous meningitis. These cases are found both in children and adults.

III. Meningeal Form

(*Tuberculous Meningitis, Basilar Meningitis*)

These cases have a well-defined *prodromal stage* during which the diagnosis can be made and the prognosis given. The symptoms of this stage include *irritability* of the child, *sudden vomiting, hydrocephalic cry, paralyses within the domain of the motor oculi*, the *facial* or *other cranial nerves*, later *opisthotonos*, increasing apathy, at times early convulsions. The *cerebral macule* (*dermography*) is present, and as I determined from an analysis of a large number of cases, death followed in seventeen days

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from the beginning of the continuous train of symptoms. The *Kernig symptom* is usually but not always present. My experience has been *uniformly unfavorable with tuberculous meningitis.* My preceptor, Didama, believed that he had one recovery in his large experience. While I was writing this chapter I saw a case which Treupel presented at a post graduate clinic in Frankfort on the Main (Oct. 25th, 1913) of a boy in whom *the spinal fluid contained tubercle bacilli, and all other elements,* including ophthalmoscopic find, satisfied him, that the case was one of tuberculous meningitis, and fully recovered.

The statement has been recently made (London Lancet), that *one in 200 cases of tuberculous meningitis recovers.* Pitfield reports *29 cases* (one of his own) from medical literature which recovered. In 10, necropsies confirmed the diagnosis, in 18 tubercle bacilli were found. McCarthy in several reports of the Phipps Institute states that he frequently found evidences of healed tuberculosis of the nervous system in persons who ultimately died of phthisis pulmonalis. Others hold that the prognosis of tuberculous meningitis is not absolutely bad and base their conclusions upon the post mortem evidences of healed meningeal tuberculosis. The incidence of cure among the thousands of reported cases is so slight that in offering a prognosis it deserves but insignificant consideration.

Tests

Tuberculin Tests.—In all forms of positively diagnosticated acute miliary tuberculosis the tuberculin tests, preferably *von Pirquet, Calmette* and *Moro,* will in the overwhelming majority of cases give negative results. Tuberculous meningitis rarely reacts to these tests; my experiences prove them negative in over 90 per cent of all cases. The *typhoid type* is almost *uniformly negative* to the skin and ocular tests; injections of tuberculin are contraindicated. *Negative tuberculin tests* above mentioned, in *cases positively tuberculous* (acute miliary tuberculosis), argue in favor of unfavorable prognosis.

The ophthalmoscope offers positive information in over 75 per cent of cases of miliary tuberculosis and should therefore be used for diagnostic and prognostic purposes, in this and in all forms of miliary disease.

The study of the opsonic index is of indifferent or slight value for prognosis of any form of tuberculosis, and is unavailable for general use. (Bandelier in Roepke, l. c.)

Lumbar puncture is of positive prognostic value, for it clinches the diagnosis in doubtful cases very often, when tubercle bacilli are found in clear fluid as a rule under high pressure, with the presence of lymphocytes. It must be remembered that the latter may be present with congenital syphilis also.

Sugar in the Cerebrospinal Fluid.—Connall, who has given this sub-

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ject great consideration, has examined 122 specimens from 69 cases of tuberculous meningitis and reports his results as follows:

"In tuberculous meningitis sugar was found to be present in the great majority of the cases, and at all stages of the disease; 122 specimens were examined. An active reduction on boiling of the Fehling's solution occurred in 15, a partial but decided reduction in 102, and no reduction at all in only 4 instances. Complete absence of sugar was observed in only 2 cases. It was noted in the last week of illness, three times in one case and once in the other, and in each case at other times there was a slight reduction of Fehling's solution." Jacob concludes that "In tuberculous meningitis sugar is present, except in very rare cases shortly before death, in which stage difficulty of diagnosis rarely exists." While the presence or absence of sugar is of some prognostic value, it is not of the same significance as in cerebrospinal meningitis.

The majority of children who die of tuberculous disease between the first and fourth year fall victims to tuberculous meningitis; 40 per cent of these die during the first year of life and 60 per cent after. This high mortality is reduced with advancing years. In 70 per cent there is an hereditary predisposition. Koch (Bandelier and Roepke) reports 355 cases of tuberculous meningitis in which 130 had measles and 67 whooping cough preceding the tuberculous infection. The proportion of adult tuberculous meningitis to the infantile is 1 to 7.5 (8 to 60 cases).

2. *Pulmonary Tuberculosis*

(*Pulmonary Consumption, Phthisis pulmonalis, Phthisis tuberculosa, Schwindsucht* [*Lungen*])

All lung diseases due to the Bacillus tuberculosis are included in the group of pulmonary diseases known as *consumption* or *phthisis pulmonalis.* We will consider the prognosis of the disease basing our conclusions on the following classification:

I. Acute pneumonic tuberculosis (lobar or lobular).

II. Chronic pulmonary tuberculosis (ulcerative and caseating).

III. Chronic fibroid phthisis (chronic tuberculous pneumonia) (tuberculized pneumonokoniosis).

In all forms of lung tuberculosis we are dealing with complex problems and changing elements which must of necessity influence prognosis. It may be said that the *extent and location of the tuberculous process,* the *virulence* of the infecting agent, the many general factors already considered, including *predisposition* (acquired and inherited), associated *clinical manifestations* which show the *resisting power* of the infected, the *stage of the disease,* the ability of the patient to take advantage of *conditions which offer an obstruction* to the onward march of the disease and stimu-

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late the reparative and protective processes, with many other factors, together and alone, influence the forecast decidedly.

I. Acute Pneumonic Tuberculosis

There are unquestionably cases of acute tuberculosis in which the deposit is limited, where there are indefinite symptoms during a short period, slight febrile movement, insufficient physical signs to make localization possible, languor and anorexia which yield. Nature comes to the rescue. *Calcification* or *fibroid change* in these limited areas are responsible for many healed and circumscribed lesions which are included in the post mortem findings in many who finally die of non-tuberculous disease and also for many positive tuberculin reactions. In these cases, which Sir A. E. Wright might include among the *local infections,* it is possible to *raise the resistance* of the patient sufficiently "to cause the *infection to disappear*" and present fresh infection. Wright contends that "the method of following the progress of an *anti-tuberculous immunization* lies in the observation of the *opsonic capacities of the serum.*" Patients in whom the *deposit is limited* show a *low opsonic index;* when the process is active, it is occasionally high and irregular.

(a) Lobular Pneumonic Tuberculosis.—Acute pneumonic tuberculosis in which there are physical signs of tuberculous bronchopneumonia is a virulent infection, most frequent in children, and usually associated with rapid loss of strength, cyanosis, hurried respiration and cough. There may be hemoptysis, and but few or no tubercle bacilli, depending upon the stage of the disease, evidences of constitutional disturbances and death in from two weeks to several months. It is surprising to note how long some of these patients tolerate the high temperature and the rapid pulse. A chronic stage follows, and months of fever, with extreme wasting, dry unsatisfactory cough, with night sweats, may precede death. In some there is laryngeal invasion finally, which makes the end painful. *A reversal of the usual type of hectic fever* in acute *tuberculosis, high morning temperature* and *nocturnal fall,* is indicative of rapid failure and early death.

The acute *galloping consumption* which may be either lobar or lobular (often of the mixed type, with far-reaching miliary deposit, infiltrating tubercle and in some cases coalescence of the smaller miliary deposits) offers an unfavorable prognosis and is likely to be of short duration. It is also frequent in children following respiratory infections, measles, whooping cough or a long period of latency, in which the bronchial nodes were primarily infected. *Hemoptysis* is occasionally the first symptom of the disease; acute symptoms of pneumonia may follow and progression may be rapid. With this history it may be safely concluded that there existed for sometime, without symptoms, a latent or partially healed but limited focus which was "opened" and the spread of the disease followed. A large num-

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ber of these acute cases are hurried to the end by the intolerance of the stomach and intestines. *Tuberculous dyspepsia* makes impossible the nourishing of some of these cases which become sub-acute, emaciation is rapid, heart insufficiency prompt, fever high—all conditions which invite early death.

The duration of the galloping cases (acute pulmonary miliary tuberculosis) is between 12 to 15 days and two to three months, averaging about seven weeks.

(b) Lobar or Pneumonic.—In these cases there may suddenly develop all of the symptoms of an *acute pneumonia (lobar)*; unless there are evidences of previously existing tubercular foci, the true pathologic conditions may not be suspected. There may be, as I found in one case which I reported (Elsner) a sudden chill, high fever and suspicion of an apex pneumonia. There were pneumococci in abundance in the rusty sputum, the time for crisis passed without a change of symptoms, the hope for lysis was abandoned after ten days of unchanging conditions. The sputum continued free, there were evidences, after the twelfth day, of mixed infection, tubercle bacilli and the Fraenkel cocci were abundant. Close questioning proved that several years before his present illness the patient had an *ischio-rectal abscess* and this was the source of infection. Death resulted several months after the initial pneumonic tuberculosis, with cavity formation and other evidences of general tuberculous infection. There is in most of these cases an *old focus* which has been lighted into activity; *infiltrating tubercle results;* large areas are included or one lobe only is involved. With this there may also be miliary deposit. In the article which I mention above (Elsner), reference is made to *pneumonic tuberculosis* following *aspiration of blood from germ laden cavities,* after hemopytsis, as originally suggested by Baumler, to distant parts of the lung. Either pneumonic or bronchopneumonic tuberculosis may be thus spread, and an acute process developed in the midst of chronic phthisis. *It is possible for pneumonic herds to be produced solely by tubercle bacilli, without mixed infection.* It occasionally happens that these types of *acute pneumonic phthisis heal or fall into long periods of latency.* One must not conclude that the prognosis is absolutely bad. A recent experience (1911) has been encouraging. A priest, age 45, developed all of the classic symptoms of pneumonic tuberculosis (lobar) with positive bacteriologic find, with irregular fever and progressive emaciation and rapid pulse. To all who saw him the case seemed hopeless. In this condition he was transferred to St. Gabriel Sanitorium in the Adirondacks and there made, so far as we can judge from present indications and physical examination, a full recovery with a gain in weight of over fifty pounds. What the future has in store for such patients we are not able to tell, but with the experience of the past already forewarned, early attention to symptoms, if any recur, may lead to satisfactory results.

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In all cases of pneumonic tuberculosis a guarded prognosis must be given, the fiery and acute cases will most of them fall victims to the virulent toxemia, a number may live for a long time and ultimately die of chronic or subacute phthisis, others will enjoy long periods of latency, while the happier outcome of cure is a possibility and should encourage the therapeutist to take advantage of modern methods even in desperate cases. My clerical friend has remained without symptoms to the present time, the picture of health.

II. Chronic Pulmonary Tuberculosis

(*Ulcerative and Caseous*)

The chronic type of pulmonary consumption is the most frequent of all lung invasions. With this, as in all diseases, as I am continually endeavoring to impress upon my readers, prognosis is nothing more than the conclusions which we reach from thorough detailed and refined diagnosis. A large number of these cases are curable, many become latent; the vital fact which interests us in considering their future is that they can only be saved by *early diagnosis and prompt treatment. Put in the resistance, bring the condition of the patient to par or above, and the disease, if in its incipiency, will be stayed and cured in over 80 per cent of all cases, while 20 per cent of all forms of the disease are saved. To wait for definite physical signs before making the diagnosis darkens prognosis, for the patient's chances are reduced thereby. To anticipate the final development in cases which are strongly suggestive, adds to the patient's chances. Positive physical signs are never early evidences of lung invasion; they mean that the case is advanced.*

Symptoms and their Prognostic Value

The prognostic significance of symptoms may be summarized as follows:

Cough.—Cough, which is not promptly controlled by the usual methods of treatment, particularly if dry and hacking, which during the early morning hours may be followed by the expectoration of only a small pellet of sputum, which on examination gives negative results, which may or may not be accompanied by slight rise of temperature, usually some lassitude, is always strongly suspicious of tuberculosis. *Cough with increasing muco-purulent expectoration* is evidence of *advanced disease* and as a rule *tubercle bacilli are present.*

In all cases of cough having no other symptoms to make diagnosis positive, the sooner such cough is considered to be due to tuberculous deposits, the more the prognosis is improved. To wait for the appearance of tubercle bacilli reduces the chances of the patient. Some of these patients at

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first cough only once or twice during the early morning hours; the cough is due to the irritation of a focus still "closed."

Each day of cough with changing sputum, increasing evidences of bronchial irritation, robs the patient of resistance and lowers his chances of recovery. Cough may continue during weeks with no sputum, even in rapidly advancing cases in which miliary deposit predominates, but in these cases there are usually other evidences—fever, emaciation and accelerated pulse—which are strongly suggestive. These cases offer a less favorable prognosis than do those in which, from the beginning, there are none of the symptoms of miliary deposit, though these are by no means hopeless. Cough with *nummular expectoration* is always evidence of advanced disease. Tubercle bacilli will be found in such expectoration without long search.

Cough with increasing infiltrating deposit of tubercle may in some cases be slight, as a rule it is troublesome. *Large areas of lung tissue may be infiltrated without cough.* This is not a frequent anomaly but it does present; failure to recognize the true pathologic condition, postpones diagnosis and materially influences the outcome.

With *cavity formation* there is usually abundant purulent and nummular sputum, likely to be periodical, most abundant in the morning. Such sputum and cough are unfavorable. Besides tubercle bacilli, there are evidences of mixed infection. If the sputum shows besides, benign saprophytes, other bacteria which are pathologic, the prognosis is accordingly influenced. *The presence of the tubercle bacillus in the sputum* is proof positive of a disorganizing process; there has been breaking down of tissue, the disease has become *"open"* and is beyond the incipient stage. The prognosis is therefore less favorable, for in those cases (barring acute *miliary tuberculosis*) which are "closed," where there are no physical signs of disorganization or tubercle bacilli in the sputum, recovery follows rational treatment in between 85 and 90 per cent of cases; the time required for a cure is materially shorter than in the more advanced cases. *Large numbers of bacilli* are unfavorable when found in single fields. The *beaded appearance of bacilli* has been variously interpreted by clinicians. Many hold the beading to be favorable. My experience does not justify that conclusion, as I have found this oftenest with acute or rapidly advancing disease. This may ultimately prove to have been mere accident. *Elastic fibers* are evidences of disorganization.

Shortness of Breath.—Shortness of breath with uncontrolled cough, few or no physical signs, no evidences of existing lesion in any organ accounting for the symptom, should be interpreted as due to tuberculosis. If there is no emaciation, a good family history, but little or no fever, fair circulatory condition, such cases offer a fair prognosis if treated early. Shortness of breath is not always evidence of the extent of the tuberculous process. With existing anemia, weak heart muscle, particularly in young

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girls, or in some cases of mixed tuberculosis (i. e., miliary and infiltrating), shortness of breath on slight exertion may be out of proportion to the extent of the disease. Shortness of breath with increasing loss of weight, rapid pulse and persistent elevation of temperature is unfavorable.

Bronchial Hemorrhage.—The occasional admixture of a "streak of blood" should always lead to the suspicion of possible ulceration, erosion of a capillary, or disorganization of limited extent. The "streak" may be the fore-runner of a large or small hemoptysis. It may in some cases mean nothing at all.

Hemoptysis, large or small, is always proof of an open focus, hence an active process. It is by no means always followed by an increase of symptoms or progression of the disease. In many cases it is the *first evidence* of existing tuberculosis, has been the signal which the clinician and patient heeded which proved fortunate, for it may lead to full recovery. Even cases with positive evidences of deposit in one or both apices, in which hemorrhage was the first expression of existing disease, have been cured or halted by timely intervention. There is no stage of tuberculosis in which hemoptysis may not occur.

Death, the direct result of hemoptysis, is exceptional. The erosion of a large vessel, usually an artery in the advanced stage of the disease, has occasionally caused sudden death.

Hemorrhage may in some cases lead to anemia by recurring at short intervals or because of its profusion.

The immediate effect of hemoptysis is to frighten and depress; unless the loss of blood is considerable, reassurance promptly suffices to return the patient to his previous condition. *Large hemorrhages repeated at short intervals,* usually in the advanced stage of the disease, naturally rob the patient of resistance, weaken the heart and, if aspiration *bronchopneumonia* of mixed type or tuberculous pneumonia results in distant parts of the lung, the condition may become serious and threatening. In occasional cases there is a depressing *fever* following hemoptysis which may continue for several days.

There are cases in which for some reason the *tuberculous process advances rapidly after hemorrhage* and disorganization promptly follows, causing cavity formation with high fever, rapid pulse, mixed infection and death in a few months. If the changes are limited to the dependent portions of the lung, we assume, as already suggested, that infection was spread by aspiration.

It is safe to conclude that *hemoptysis* not otherwise explained *is of tuberculous origin,* that it does not lead to tuberculosis, but is evidence of an existing focus. Franz Stricker's statistics prove 86 per cent of hemoptyses tuberculous where the bleeding came on without known cause.

Fever.—Fever is a symptom of enormous prognostic values. Rise of temperature which is not modified or controlled by rest and suitable sur-

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roundings argues in favor of overpowering toxemia and insufficient resistance, and is always unfavorable. *Slight evening rise of temperature in incipient cases deserves prompt consideration, whether associated with positive physical signs or not. Its disregard as a symptom of early tuberculosis, leading to procrastination, is always against the interest of the patient.*

The effect of *short* but *repeated febrile attacks without positive symptoms,* usually diagnosticated as *influenza or malaria,* often burden the history of the tuberculous subject when he presents with continuous and positive symptoms. Latham adds to these the history in many cases of "feeling tired," "not really fit," without having consulted the doctor. These short periods of fever of doubtful significance originally prove to be of tuberculous origin and most of these subjects present with reduced resistance and positive physical signs of advanced disease.

When such cases develop *continuous fever, sweating, with accelerated pulse,* the prognosis is accordingly influenced.

The temperature curve is an expression of the behavior of the tuberculous process; it must always be thoroughly considered in offering a forecast in the individual case. If fever persists the process is not under control or there is some wearing complication.

Early morning rise of temperatures is always ominous; if in cases where it is present there is gradual increase during the day, with accelerated pulse, unless controllable, it is also of serious import; such cases fail rapidly. *Intermittent fever,* usually a decided chill, or chilly sensation during the afternoon followed by fever and later *night sweat,* is evidence of *mixed infection,* pyogenic as a rule, and does not complicate incipient chronic tuberculosis. It may in some cases prove expressive of associated miliary and spreading infection. *Night sweats,* unless due to some non-tuberculous complication, unfavorably influence prognosis. There are cases of chronic tuberculosis which yield after the appearance of night sweats, an experience which justifies persistence in the treatment of chronic phthisis.

Frequent daily measurements are absolutely necessary in all cases of chronic tuberculosis, that valuable deductions as to the true condition of the patient may be obtained.

Hectic fever wears the patient, weakens and depresses, and is always evidence of failing resistance; the reparative powers have been exhausted. *Anorexia* during prolonged periods with slight fever and *loss of weight* is unfavorable. In these cases, with intolerant stomach, powerful and helpful factors are withdrawn and the patient's chances reduced.

Diarrhea.—Early or late diarrhea is unfavorable. When early, if controllable, it is not significant of intestinal invasion; if not controllable, it remains a weakening factor. *Late colliquative* diarrhea depletes and *hastens* the end. The *presence of tubercle bacilli in the stool* of tubercu-

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lous subjects is not positive proof of intestinal tuberculosis. Sputum is easily swallowed or bacilli may be washed into the stomach with food and drink. With *persistent diarrhea, tubercle bacilli and characteristic stool, ulcerative tuberculous enteritis* may be diagnosticated and offers an unfavorable prognosis.

Pain.—Pain is usually an expression of *pleuritis sicca;* if more serious forms of pleurisy (effusion, chronic pleurisy, empyema, hydro and pyothorax pneumothorax) are not among the complications, it is of no great significance and is transitory.

The *misshapen or retracted thorax,* with a previous history of pleurisy or pneumonia or suspected latent tuberculosis, with adhesions or retractions due to the formation of fibrous tissue formed in the process of healing and positive evidences of fresh infection or exacerbation of existing disease, require consideration and deserve to be weighed in offering prognoses. *Limited expansion of the thorax* in cases not too far advanced may be materially increased by pulmonary gymnastics in a favorable climate, thus adding to the patient's chances.

The Heart.—The small heart of the tuberculous subject has been previously mentioned. *Abnormal irritability of the heart, erratic behavior* under stress, is not uncommon even in favorable cases. Hearts remaining rapid under rest and favorable conditions, with or without fever, suggest advance of the process. If there is *fever with rapid heart* which is not controllable, at the same time *gradual loss of weight,* the disease is not under stress, is not uncommon even in favorable cases. Hearts remaining is unfavorable.

Blood pressure study proves chronic tuberculosis to be a *hypotensine* disease (80-90 mm. Hg.). Sudden or gradual fall of blood-pressure, with or without evidences of advancing disease in physical signs, needs to be watched and is not encouraging.

Emaciation; Weight.—Chronic tuberculous subjects, when brought under favorable conditions, if they are doing well, should show a gain in weight. *In no subject who is losing weight has the disease been brought under control.* Weekly or semi-weekly weighing offers valuable indications for prognosis.

Pye-Smith says: "To put the matter briefly, I would say that, beside family history, the less important facts for prognosis in phthisis are those which concern the lungs, and the more important those which concern the whole body. While a patient puts on flesh and is free from fever, he is doing well, whatever takes place in his chest; while he is losing weight, and suffers from anorexia, sweating, diarrhea and hectic, he is going down hill, however little sign of disease auscultation of his chest may show."

Muscular weakness, atrophy, exalted superficial reflexes are likely to indicate advancing diseases, though by no means dependable prognostic factors.

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Hoarseness, persisting, means either *paralysis* of the *vocal cords* or invasion of the larynx, usually ulceration of the anterior surface of the posterior laryngeal wall. *Tuberculous laryngitis* as a complication of chronic phthisis is always of the gravest import, decreases the patient's chances of recovery and leads to weeks of suffering which is uncontrollable, and usually a painful death. No other condition is more likely to impress the physician with the limitations of his art.

The subject of Tuberculous Laryngitis will be given special consideration.

The Urinary Organs.—*Albuminuria* is not, when transitory, of serious moment. In the later stages of the disease, with *casts,* and occasionally *hematuria* it may be an expression of either *amyloid degeneration* or *tuberculous nephritis,* when it is a symptom of serious and widespread disturbances. The *addition of general dropsy* is evidence of the terminal stage of the disease.

Blood-pressure with degenerative changes in the kidney is low in proportion to the weakness of the heart muscle and the associated amyloid changes in the arterial walls.

(*Renal tuberculosis* will receive separate consideration.)

The Diazo-reaction (Ehrlich) is of positive prognostic value. Often present in chronic tuberculosis, if found early, it is likely to disappear as the process is brought under control and the patient improves. Persistence of the reaction after once found in severe cases (not all cases react) is with but rare exception an indication of an uncontrollable and progressive tuberculosis.

There is a *rheumatoid form of tuberculosis* associated with chronic lung invasion, fully described in an exhaustive monograph by Poncet and Leriche which is obstinate, usually becomes chronic, and adds to the sufferings of the patient besides lowering vitality.

Liver and Spleen.—Invasion of the liver and spleen, tuberculous deposits of *amyloid* degenerations do not argue favorably for the future of the tuberculous patient. These are usually terminal complications and are not limited to the organs mentioned, but are likely to involve bone and, as already mentioned, the kidney. The usual changes in *blood-vessels,* characteristic of amyloid disease, with other factors lead to *anemia, dropsies and diarrhea.*

The Digestive Organs.—The *influence of purulent discharges* on the prognosis of chronic tuberculosis has been a source of controversy and disagreement in the past. Many of the older writers believed that the discharge from an *ischiorectal abscess,* usually a tuberculous process, had a wholesome and a restraining effect on pulmonary tuberculosis. That chronic phthisis may be complicated with chronic ischiorectal infection during many years without evident influence is true. The safest conclusion for us, in the light of modern knowledge, is that any tuberculous focus

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within reach should be promptly removed; the patients' chances are not prejudiced thereby, but rather improved.

Tuberculous peritonitis complicating phthisis pulmonalis is always serious, but with abundant *ascites* is not always fatal. I number such cases among my tuberculous patients who made satisfactory progress in whom *abdominal section* led to cure of the peritonitis and the lung process was either uninfluenced or in an encouraging number became latent.

The Nervous System.—The nervous system, barring tuberculous meningitis, considered in connection with acute miliary tuberculosis, and occasional cerebrospinal meningitis, offers but few indications which materially influence prognosis. I have met a number of *peripheral neuritides, neuralgias, some suddenly arising hyperthyroideas, paresthesias, anesthesias* and finally *mental disturbances, insanities,* including *melancholias.*

With the dissemination of knowledge concerning tuberculosis, the natural hopeful tendency of the consumptive has been encouraged and there is no longer in the incipient stage the depression which formerly followed immediately after the diagnosis became known; on the other hand, most patients to-day begin to make arrangements which they fully expect will lead to a happy termination.

There is a wholesome *autosuggestion* which, if encouraged by every possible means (environment, etc.) proves an important factor in leading the patient toward recovery.

The Blood.—*Chlorosis and anemia invite tuberculosis.* Increasing chlorosis and anemia are indicative of extension of disease or some associated depressing factor which is retarding the progress of the patient. *Anemia with edema or other dropsies is always unfavorable.*

The *blood condition* may be considered favorable when the number of red corpuscles is not materially reduced, leukocytes unchanged and hemoglobin but slightly diminished. This is the blood condition which is found in the incipient stage of the disease. Grawitz, as the result of his observations found, with advance to the *second stage,* without fever, erythrocytes unchanged, slight increase of leukocytes with hemoglobin, as in the first stage. In the *third stage,* with fever, less favorable, there is a marked reduction of red corpuscles, decided increase of leukocytes with marked reduction of hemoglobin.

The *blood platelets* are materially increased in number in tuberculosis.

The rapid *rise of the leukocytic count* is always unfavorable, for it is indicative of advancing disease with mixed infection, such as is found in the terminal stages of the disease.

In women, *early chlorosis* must be expected in many cases. A rise of *color index* is favorable.

Increase of *eosinophilia* in the blood and sputum has been found by many to be coincident with improvement and their absence or decrease marked, when there are exacerbations or the disease progresses.

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Arenth believes that the simple counting of white blood corpuscles is of no value for diagnostic or prognostic purposes and has made exhaustive studies of the blood picture, more particularly *the differential count of the polymorphonuclear neutrophils* with regard to *the number of their nuclei.* Six classes are recognized according to the number of contained nuclei. *With infectious disease Arenth found, in tuberculosis particularly, that the number of nuclei in the cells is decidedly reduced in unfavorable* cases; in those without resistance there is a *preponderance of cells with one or two nuclei only.* In the *favorable* cases, the percentage of leukocytes holding three and more nuclei is increased. In bad cases Arenth therefore contends, and clinical experiences strengthen his contentions, that "there is a shifting of the blood picture on the left, i. e., one or two nuclei." ("Verschiebung nach Links.") The blood picture, therefore, shows, "as against the normal (25 per cent mononuclear, 75 per cent polynuclear leukocytes) an enormous disproportion in unfavorable cases; increase of mononuclears and decrease of polymorphonuclear cells."

Ringer and Minor have given some interesting data including their experiences with the "Arenth leucocytic picture in pulmonary tuberculosis and its prognostic value." The first mentioned made 729 counts in 475 patients. They divided their cases according to the extent of the lung invasion into four groups.

1 Good. 2 Medium. 3 Bad. 4 Very bad. Going over their counts they found that the one and two nuclei cells were most frequent in the "bad" and "very bad" groups and decreased in the "good" and "medium" groups. In a small number of cases they found with a good clinical symptom complex, a very bad blood picture and "noted that shortly thereafter the patient took a turn for the worse." Ringer concludes that the Arenth count "is of a certain value, should not be abandoned and it will, in certain apparently favorable cases, correctly presage an unfortunate outcome, or vice versa." The Arenth blood picture gives no indication of the extent of lung invasion nor of the stage of the disease; *it is, however, an index of the resisting power of the patient.*

Solis Cohen and Strickler conclude (quoted by Ringer): "While the average index showed little change, in most of our individual cases the proportion of cells in the first two classes of Arenth seemed to be increased as the patient improved, and in a number of cases to be decreased as the patient grew worse." Of 27 improving patients whose blood was examined more than once, an increase in cells with one and two nuclei was observed in 22, and a decrease in 4. Among advancing cases there was an increase in 3, a decrease in 4, and no change in 2." The figures of these observers are opposed to those of others. Differences in methods of counting the nuclei, a difficult process, must naturally be considerable. Miller and Reed, after considering the subject and making a large number of counts, believe that "the Arenth blood picture is of real value in prog-

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nosis." Miller and Reed report further that cases of pulmonary tuberculosis which are doing badly, progressive or exacerbating, show the following blood changes:

(a) Leukocytosis.
(b) An increased percentage of neutrophils.
(c) A diminished percentage of small lymphocytes.
(d) A diminished percentage of eosinophils.
(e) A marked shifting to the left of the Arenth blood-picture conversely, changes in the opposite direction if any of the above factors are favorable.

I fully agree with Ringer, that those who use the Arenth method will continue to use it, that it is simply one link in a chain which strengthens prognosis, that blood pictures will never displace bedside findings including physical signs, that "he who places implicit confidence in its readings and bases his prognostic opinions chiefly thereon, will not infrequently be led into error."

The *persistence of tubercle bacilli* in the blood is always ominous. The more severe the infection, the nearer its termination, the more certain are we to find bacilli in the current. We do, however, find tubercle bacilli in the blood stream in incipient cases; but this is transitory as a rule.

Liebermeister's far-reaching study of this subject justifies *conservatism* before we conclude positively that the bacilli are true tubercle bacilli, for acid-fast bacilli were found by him in many non-tuberculous diseases in the blood, in children who did not react to tuberculin and in those apparently healthy. The fault lies in technique. Bandelier-Roepke conclude: "The significance of bacillemia in tuberculosis is not yet settled and positive conclusions are not justified."

The value of the *opsonic index* in the prognosis of tuberculosis has been considered in this chapter; as already suggested, the busy clinician will be unable to take advantage of it; in acute cases it may prove to be more valuable than in the chronic.

Physical Signs

Physical signs and stage of the disease must of necessity influence prognosis. It has been my object throughout this chapter to keep before the mental vision of the physician and student the enormous value of early recognition and its influence on prognosis. In the United States we consider *"incipient cases"* those with but slight or "no constitutional symptoms (including particularly gastric or intestinal disturbance or rapid loss of weight); slight or no elevation of temperature or acceleration of pulse at any time during the twenty-four hours."

"Expectoration usually small in amount or absent."

"Tubercle bacilli may be present or absent."

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"*Slight infiltration limited* to the apex of one or both lungs or a small part of one lobe."

"No tuberculous complications."

Every *fresh extension* sufficient to make its presence manifest by positive physical signs is a menace.

The increase of *moist râles*, sputum, *bronchial breathing*, with increase in rapidity of heart, with or without decided rise of temperature, with or without tubercle bacilli, are proof of advancing disease. *Dullness over large areas*, with *bronchial or broncho-vesicular breathing*, with *moist, large, or small râles*, indicate activity of the tuberculous process.

Cavernous and amphoric breathing, metallic tinkling, marked tympany, large and coarse râles, abundant tubercle bacilli and negative reaction to all tuberculin tests, are proof positive of the *third and last stage of the disease.*

Many patients recover after fully developed *pleurisy, effusion* or even *empyema.* There is no stage save the terminal of the disease, in which a reparative process may not be stimulated; post mortems show healing processes fully established, fibrous bands, enclosing walls, the encircling and closure of cavities, the lining of pus pockets and their side-tracking, the formation of protective adhesions and a variety of processes by which nature seeks to arrest the disease, establish latency or cure it.

Every deposit which persists at the apex of one or both lungs should be considered tuberculous from the beginning, and this conclusion should not be changed until there is proof positive of error. Deposits in the dependent parts of the lung are less likely to be tuberculous than those at the apex, but these too must be viewed with suspicion until a correct pathologic diagnosis can be made.

All complications and depressing factors influence prognosis unfavorably.

Age

Age is a factor to be considered in the prognosis of tuberculosis. ***In children*** the course of the disease is rapid, as a rule, and offers a less favorable prognosis than in the adult. *Disseminated tuberculous disease,* acute miliary, including brain invasion, is more frequent in early life than later.

Prognosis is more favorable *as we advance in life;* after the 60th to 65th year we again approach the mortality and tendencies of early life. *There is no time limit in tuberculosis.* There are subjects who have been tuberculous during almost their entire lives and die of intercurrent disease late in life.

Tuberculin Tests

It will never be safe to consider the *tuberculin tests* too enthusiastically, as some have done in offering the prognosis of pulmonary tuberculosis. We do know that the reaction represents *a phenomenon of sensitiza-*

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tion; we know further that the majority of apparently healthy adults react to the Calmette, the Moro and the von Pirquet tests. The subcutaneous injection of tuberculin remains the very best method in use to-day for the detection of hidden tubercle deposit in the body. It is not without its dangers and is now used more for treatment than for diagnosis and prognosis. The conjunctival test (Calmette, Wolff-Eisner) demonstrates by positive reaction the presence of early tuberculosis in between 60 and 70 per cent of cases. Vaughn, Jr., in 160 cases of early tuberculosis, found positive reaction in 72 per cent. My figures with a large clinical material are not so high; they are in the neighborhood of 55-60 per cent. Baldwin's 67 per cent; Wolff-Eisner 75 per cent. In my practice most favorable cases of incipient disease and those in the second stage have given positive reactions to all tuberculin tests. I am using preferably the von Pirquet and Moro tests in private practice, though in a large experience with the ophthalmic test I never had an untoward experience. Others have been less fortunate. The tuberculin injection is not available in cases with fever and wasting.

Active miliary tuberculosis rarely reacts to the tests. *Positive tuberculosis of any organ* in which the tuberculin tests remain negative is less likely to progress favorably than those in which the reactions were active and positive. My experience with *tuberculous meningitis, acute pneumonic tuberculosis, tuberculous peritonitis without ascites* and often without elevation of temperature, show only a small proportion of positive reactions; the protective principles have been exhausted, the prognosis is correspondingly bad. In my tuberculous wards at St. Joseph's Hospital, where *advanced and neglected pulmonary tuberculosis* are received, it has been the rarest exception to find positive reactions.

The *von Pirquet* test for prognosis *in the adult* is valueless, the majority of healthy adults give prompt reactions. *In children* the von Pirquet shows the time of infection in cases held under observation, but is of indifferent prognostic significance.

There are *patients who fail to react during the early stage* of pulmonary tuberculosis and whom it is impossible to sensitize.

In the *presence of clinical symptoms of tuberculosis* with *suspicion that the case is advancing and a negative tuberculin reaction,* the prognosis is likely to be doubtful, usually unfavorable. I have never in my experience found positive von Pirquet, Moro or Calmette in the midst of rapidly advancing tuberculosis. Latent pulmonary tuberculosis in the adult is likely to give positive reaction to the tuberculin tests, particularly von Pirquet.

Röntgenoscopy

The x-ray in the diagnosis and prognosis of tuberculosis has become indispensable, but a word of warning against hasty conclusions by the

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inexperienced who have not learned to interpret pictures is not out of place. To be of any practical value the picture must always be interpreted *by the expert* who has trained himself by long practice for the work, and who has had abundant opportunity to compare his conclusions with post mortem finds. So many errors have been made, that many are becoming skeptical and require but little discouragement to surrender this valuable method of diagnosis and prognosis.

The more valuable results are obtained in chronic tuberculous phthisis and its associated changes. Solitary nodules and calcified deposits and glands are usually easily demonstrated. Unfortunately the Röntgen picture is not absolutely dependable for early diagnosis, and negative results or suggestive shadows deserve less consideration than clinical data, including physical signs, with a thorough consideration of all that the case offers.

Valuable data concerning the condition of the *bronchial nodes* for diagnostic and prognostic use are given by x-ray examination. This area (hilus-bifurcation of trachea) is often suspected in cases where indefinite symptoms have followed the infections of early life, including measles, pertussis, pleurisy, lymphatic enlargements of the neck, and the true condition, if revealed early, may prove life-saving.

Pleural effusion and *nodular deposit, displacement of thoracic viscera,* the *size and position of the heart and diaphragm,* all important, are frequently corroborated by x-ray examination. These conditions, with their influence on the progress of the individual case, can as a rule be studied and recognized without x-ray examination. There never will be a time when the well-balanced physician will surrender the results of painstaking physical examination in favor of the revelations obtained from the Röntgenologist. The Röntgenologist demonstrates shadows only; what these are, what they mean to the pathologist and diagnostician, what their value for prognosis, is not easily determined and once more I must insist that the cautiously taken history, with a full consideration of the subjective and objective manifestations in the individual case, are needed to obtain rational and valuable data for prognosis.

The Tuberculosis of Early Life

The tuberculosis of children as it invades the lung is more likely to be *disseminated,* less likely to limit itself to the apices, is therefore often characterized by the more serious features of *miliary deposit.* The active disease in many is preceded by *glandular enlargements* and *caseation,* particularly of the cervical glands, and we ought never to forget the enormous etiologic importance of the *bronchial lymph-nodes.* These may have been previously infected or the deposit of bacilli may take place during or follow any of the acute infections of early life. *Changes in the mesenteric*

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glands with *peritoneal invasion* are not infrequent. These cases are always serious. Invasion of the *bones and joints* is more frequent than in the adult and precedes pulmonary tuberculosis in most cases.

The *development of amyloid disease, dropsies,* and *enlarged spleen* is, in children with bone and pulmonary tuberculosis, characteristic of the last stage of the disease. The prognosis in children is materially influenced by *contact with tuberculous parents.* The mortality of early life has been changed by the improvement of social conditions; statistics will be still more favorable when there is a concerted effort which will make it possible to place the children of the active tuberculous in normal surroundings. This not only influences the mortality of childhood, but will prevent latent deposit which may become active during the mature years of life. Other features of prognostic value influencing the tuberculous disease of the lung in children have been considered in the preceding pages. Attention has been called to the frequency of tuberculous meningitis.

Marriage

As already shown, *contact with tuberculous parents* increases at once the chances of infection. Mothers who are tuberculous are a menace to their offspring; their children are more likely to be infected than are those of tuberculous fathers. The *suckling of the tuberculous mother* in whom the process is active is likely to develop some form of infection. I have been surprised to note the frequency of tuberculous meningitis under such conditions. The infection of the child is usually early. *Latent tuberculosis* in the mother is often lighted to activity by *pregnancy and childbirth.* The extension or activity is greatest during the last half of pregnancy.

My experience does not justify the nursing of a babe by a mother in whom the process has recently been arrested. Both will be likely to develop active tuberculosis. One of the most serious complications during pregnancy or lactation is *tuberculous laryngitis;* this may develop in the mother in the presence of only limited lung disease. *The prognosis is absolutely bad;* the progress is rapid, with disorganization, painful ulceration, and edema of the larynx. Dubois says: "If a woman threatened with phthisis marries, she may bear the first accouchement well; a second with difficulty, a third never." Weinberg has shown that *still births* are increased 50 per cent in tuberculous mothers. *Abortion, miscarriage,* either criminal or spontaneous, increase the risk to the mother and invite the onward march of the disease.

Subjects who have *healed tuberculosis* are likely to beget children who are ultimately burdened with some form of tuberculosis. *Environment* and *social condition* must of necessity remain important factors in the consideration of the influence of the tuberculous parent on offspring.

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Complications

Diabetes complicating tuberculosis, whether acquired after or before infection, is always serious and finally leads to death; usually the diabetes is pre-existent. The association of **chronic alcoholism** and tuberculosis is always unfavorable, the latter process seeming to advance with unusual rapidity, tissues are non-resistant and are ready to break down on slight cause. Tuberculous or non-tuberculous **meningitis** is often the cause of death.

Exophthalmic goiter, typical and atypical, may materially influence the prognosis. Brandenstein found in his clinical material in Hamburg that 20 per cent of the male tuberculous and 33 per cent of women had enlarged thyroids and 20 per cent of the men and 28.5 per cent of women showed positive evidences of exophthalmic goiter.

Gangrene of the lung is always of serious significance. It is a late complication, usually appearing when the disease has advanced to cavity formation and, with added symptoms of sepsis, often delirium and a typhoid condition, the patient dies.

The **obese** who develop tuberculosis offer little resistance as a rule. They are inclined to be *anemic,* the myocardium is promptly weakened and the disease usually advances rapidly with increasing evidences of *cardiac insufficiency.*

Gouty conditions do not influence tuberculosis unfavorably; with these there is greater tendency to *fibroid* change in the lung and chronicity.

Syphilis, particularly neglected cases with lowered resistance, offers a favorable medium for the advance of tuberculous disease. Tuberculosis is never favorably influenced by the addition of syphilis. It is not unusual to find acute tuberculosis shortly after syphilitic infection, and to see the rapid advance of the chronic form of the disease as well as the kindling of latent deposit to activity. If, on the other hand, tertiary syphilis is present and tuberculosis is acquired, the course of the latter may be uninfluenced by the previous specific infection. The French have claimed a favorable influence on the tuberculous disease by the exhaustion of the syphilitic poison and the ultimate tendency of the tuberculous process to fibrosis and chronicity.

That there are many cases of tuberculous disease of the lung and syphilis combined, in which we find not only positive bacteriologic evidence of the former, but establish the certainty of the latter by sero-diagnosis, in which the *mixed treatment* (salvarsan and anti-specific drugs) gives satisfactory results which cannot be denied. The clinician is frequently surprised to find his prognosis favorably influenced in such cases by systematic and specific treatment.

In the presence of tuberculous invasion of the lung, *specific treatment* and the *Wassermann test* are often justified, and should be used for their diagnostic and prognostic value.

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Tuberculous pleurisy will be separately considered; it is rarely absent where lung deposit is superficial.

Pneumothorax due to the perforation of the lung, because of superficial cavity formation, is a frequent complication and may lead to sudden death. It may occasionally arise from the rupture of a superficial emphysematous patch. If *pyopneumothorax* follows, there may be a period of acute symptoms, exacerbation with high fever, rapid pulse and death, or the patient may rally and fall into a chronic condition in which all physical evidences of pus and air in the pleural cavity continue, or he may add to his weight and live for a number of months. In a proportion of cases, if the disease is limited to one lung, the occurrence of pneumothorax may stimulate reparative processes, particularly fibrous growth, and prove salutary. Those cases in which the lung process shows early tendency to disorganization with *acquired pneumothorax* are not among the favorably influenced by the accident. One-half of all pneumothoraces are tuberculous.

Atelectasis may, if widespread, seriously interfere with the condition of the patient. It is caused by the occlusion of one or more bronchi, usually by cheesy masses, either formed *in situ* or transported from another part of the lung. Naturally the area supplied by the included bronchus collapses and the patient is robbed of the breathing surface. If there is much associated consolidation, the condition proves promptly serious; otherwise compensatory efforts are sufficient to relieve the embarrassment. *Emphysema* may result from the expansion of the lung in the neighborhood of tuberculous infiltration; its importance depends on the extent of the primary disease, its stage and the ability of the heart to come to the rescue. As a rule *limited emphysema* need cause but slight concern.

Purpura with pulmonary tuberculosis is always a grave symptom; it is likely to be associated with the end or cachectic stage of the disease. In some, it is an *evidence of acute exacerbation* and is not infrequently associated with active febrile movement and with rapid loss of strength. Death may follow in a short time or, as Cruice has reported, the patient may recover.

Thrombosis is an occasional complication which may, within a few hours or days, end life. Thrombi may be multiple and extensive. Large numbers of pulmonary vessels may be plugged; at the same time one or more of the larger vessels (renal, branches of the portal or iliacs) may also be occluded. The complication is always grave.

Healed and latent tuberculosis may without known cause suddenly become active. Fresh infection is not among the impossibilities. It must be assumed that the patient in whom the tuberculous process has been halted is less resistant than the previously uninfected, and, if he is to remain free from relapse or fresh infection, he must guard himself with greater caution than is needed by the perfectly normal subject.

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III. Fibroid Phthisis

Fibroid phthisis is a tuberculous disease of the lung characterized by the development of new connective tissue. Such a process is rarely acute, almost always chronic and continues without marked constitutional symptoms during many years with consecutive change in the heart, veins, and distant organs. I will discuss the subject under the following classification:

A. Acute Fibroid Phthisis.
B. Chronic Fibroid Phthisis.
   (a) Tuberculous *ab initio.*
   (b) Non-tuberculous with final tuberculization.
   (c) Chronic interstitial pneumonia *sine* tubercle.

A. Acute Fibroid Phthisis

Cases of acute fibroid phthisis, in contradistinction to the chronic and usual form of the disease, run a virulent and rapid course. Friedrich Müller has directed attention to cases of this nature which are not usually recognized during life. They begin with outspoken symptoms, including *fever and malaise and rapid loss of strength.* The *tuberculous infiltrate is not encapsuled* by the connective tissue proliferation, but there is *prompt dissemination* and *increase of consolidation, tuberculous bronchitis* and *bronchopneumonia,* or there may be prompt development through the lymph channels of miliary invasion of both lungs. The characteristic features of the disease are the disseminated growth of connective tissue and the failure to encapsulate tuberculous herds with rapid deposit finally in both lungs, in most cases. These patients die in from 6 to 12 months and are, as a rule, between 20 and 30 years of age. Müller calls attention to the frequency of these cases, in those inherently weak, with inherited predisposition, deformed chests, after typhoid, measles, influenza, with alcoholism, diabetes, and after pregnancy.

Chronic fibroid phthisis may have *acute exacerbations* of serious import lighted by *influenza, bronchitis* or other added infections, which in many respects resemble the acute type just described with a simliar outcome.

B. Chronic Fibroid Phthisis

(*Chronic Fibroid Phthisis, Chronic Tuberculous Pneumonia, Tuberculized Pneumonokoniosis, Chronic Interstitial Pneumonia-tuberculous*)

(a) Tuberculous ab Initio.—These cases are of long duration; patients usually present a history of *acute disease of the pleura, bronchopneumonia, bronchitis or measles, whooping cough, influenza* or *other infection,* which

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has been followed by *persistent cough,* scant expectoration as a rule, during many years.

During this long period the lung process has advanced insidiously, the *fibrous growth has gradually increased, cavities* which may have existed, resulting from *chronic ulcerative phthisis,* have become *encapsuled,* the *pleura* is *enormously thickened* and, as the disease advances, one or both lungs show *cirrhotic changes* in various parts, and the lower lobes may be converted into masses of connective tissue. In some cases bacilli are long absent and the true condition can only be surmised; ultimately bacilli appear.

Chronic fibroid phthisis leads to *secondary changes* materially influencing the comfort of the patient during years before the end, which may be due to *intercurrent disease.* Among the changes are *enlarged lymph nodes, bronchial dilatation* (*bronchiectasis*), *atelectasis* and the evidences of an *overworked right heart in dilatation of the right ventricle, often dilatation and hypertrophy of the entire heart;* in the terminal stages evidences of *engorged portal circulation, enlarged liver,* with or without *ascites, cyanosed kidney, chronic gastritis, enlarged spleen and hemorrhoids.* These patients as already suggested may, under changed or favorable surroundings, live to old age. Many live 20 and 30 years after the onset, and few die before the 10th year of symptoms.

When the disease follows measles, whooping cough or rachitis in early life, it is difficult, as Miller has said, to tell what becomes of these children, for the majority are hospital inmates. If they are followed in private practice, as many are, with "chronic cough," it will be found that in middle life and later some develop or have developed chronic fibroid phthisis with dilated hearts, and the other and usual consecutive changes.

(b) Non-tuberculous Fibrosis with Final Tuberculization.—These forms, as also CHRONIC INTERSTITIAL PNEUMONIA SINE TUBERCLE, are intimately associated with conditions which continue to serve as *irritants* during many years and will receive fuller consideration in the chapters on Chronic Interstitial Pneumonia and Zenker's disease or the pneumonokonioses.

In considering the prognosis of NON-TUBERCULOUS FIBROSIS WITH FINAL TUBERCULIZATION, we must include those cases of fibroid change in the lung, either local or general, which follow *healed tuberculosis,* or are a part of the *reparative process, diffuse interstitial pneumonia, chronic broncho-pneumonia, chronic pleurisy with adhesions* and *ultimate connective tissue overgrowth in the lung,* in which tuberculization follows. These cases usually offer a good prognosis so far as life is concerned; they continue during many years before there are evidences of tuberculous infection, with all symptoms aggravated during the winter months, are materially relieved during warm weather and under favorable climatic conditions. The secondary changes mentioned under TUBERCULOUS AB

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INITIO, occurring in late stages, are likely to develop with this form of chronic phthisis. The addition of the tuberculous element influences the prognosis as a rule, duration depending upon many conditions. If there are *acute exacerbations* with fever, evidences of *tuberculous bronchopneumonia,* or if large areas of consolidation with rapid pulse and dissemination or associated miliary deposits are present, life is threatened and is usually shortened. In some cases with tubeculization there is only gradual progression; there seems to be a tolerance which prevents rapid or far-reaching deposit; the tuberculous herd is limited, may become encapsuled by the interstitial growth, and life is not materially shortened.

If the disease is complicated by *hemoptysis,* and this in turn by *fever* —an indication of *bronchopneumonia*—the process is likely in most cases to advance and undermine the strength of the patient. Even after such complications and symptoms I have seen patients fall into their previous condition of chronic invalidism and live comfortably during many years.

When there are evidences of *cardiac insufficiency* with *dropsies,* or marked changes in the *portal system* with *jaundice* (occasional), but little improvement is to be expected; death will not be long postponed.

(c) Chronic Interstitial Pneumonia (*Sine Tubercle*).—This condition is non-tuberculous and will be considered with the Diseases of the Lung. (Chronic pneumonia, cirrhosis of the lung.)

In no other disease is the physician more directly responsible for the outcome than in pulmonary tuberculosis. He must be willing to assume responsibility. Superficial examination, procrastination, failure to give the patient every advantage of existing doubt, in the incipient stage of the disease, apathy in the study of the social conditions of the sick, the lethargy of the public because of failure of the physician to educate and arouse it, remain among the leading causes of defeat.

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3. *Tuberculous Pleurisy*

It may be assumed that at least 50 per cent of all pleurisies after the fifth year of life are tuberculous. Physical signs of dry pleurisy with associated pain at the apex argue in favor of pulmonary tuberculosis and tuberculous pleurisy.

Vincent Bowditch found that, of 90 patients treated for pleurisy by the elder Bowditch, 32 and one-third finally died of tuberculosis. Barrs of Leeds reported 57 cases of pleurisy in which 21 developed tuberculosis. Salonove-Ipin had 301 pleurisies of which 84 became tuberculous. Of 88 cases treated at the Johns Hopkins Hospital, 30 later developed tuberculosis. Of 131 cases, Osler found 32 to be tuberculous (24.4 per cent) at post mortem. Landouzy claims that 98 per cent of all so-called pleurisies "due to cold" are tuberculous. Stinzing believes that over 50 per cent of all pleurisies are tuberculous. Extreme figures are given by Jakob and Pannwitz, who claim 10 per cent, and v. Sokolowski, who found only 2.8 per cent to be tuberculous. The safe figures according to an estimate made from an analysis of cases in private and hospital practice by the author, places the percentage of pleurisies positively shown to be tuberculous at 30-35.

Tuberculosis, if it follows initial (?), supposedly uncomplicated *pleurisy,* develops in an *active form* within five years in 50 per cent of the cases. R. C. Cabot in 300 cases at the Massachusetts General Hospital found 117 to have died within 5 years of tuberculosis. Hedges followed 130 cases of pleurisy treated at St. Bartholomew's Hospital and found 40 per cent with fully developed tuberculosis in seven years. As a rule, the *immediate prognosis* of tuberculous pleurisy is good; in many cases, however, the *remote prospect* becomes a source of anxiety during many years.

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The *frequency* of *effusion* with tuberculous pleuritis is shown by an analysis of Allard and Koester's material. *There were* 514 *pleurisies with effusion among* 2133 *cases of pulmonary tuberculosis. Pleurisy of early life* (before the fifth year) is not often tuberculous. Allbutt gives the incidence as 1 in 10 and "even of these the pleurisy may be only incidentally associated with a tuberculous focus, or the tubercle may be a secondary consequence of a protracted empyema."

The larger number of tuberculous pleurisies are secondary to existing pulmonary tuberculosis or are a part of general miliary infection. In cases which have every appearance of being primary the chances are that the pleural infection followed superficial lung tuberculosis which was inactive.

Men develop tuberculous pleurisy oftener than women (65-35, Bandelier and Roepke, l. c.).

Adhesions which follow dry pleurisy may have a salutary effect on the progress of *existing tuberculosis;* indeed, many with truth consider it "always a conservative and useful process" (Osler).

The formation of dense adhesions may protect against pneumothorax, may also stimulate interstitial growth and encourage chronicity.

Dry pleurisy with but few exceptions runs a favorable course. A limited patch of dry pleurisy over a consolidated area, with persistence of fever, occasional chills and sweats, must always be considered evidence of activity. Latham makes this unqualified statement: "The great majority of attacks of pleurisy in young adult life are tuberculous in nature. If this fact were appreciated sufficiently, and, still more, if all cases of pleurisy which cannot be shown to be non-tuberculous, were regarded as tuberculosis, a large number of cases of pulmonary disease would be prevented." *Cases of tuberculous pleurisy,* in which the condition is early recognized and rationally treated (sanatorium, etc.) rarely develop active tuberculosis in later life. Latham and others believe that "a greater degree of immunity is produced, and that these patients are less liable to consumption subsequently than the other members of the community." *Failure to recognize the significance of tuberculous pleurisy, on the other hand,* increases subsequent dangers, including further lung invasion.

The French report *pulmonary consumption widespread in later life in not less than* 75 *per cent of tuberculous pleurisies.*

In some cases tuberculous pleurisy may not finally be associated with more than limited and superficial pulmonary invasion, but tuberculosis of the *spine or joints* may develop or other distant infection may prove to be a serious complication. *Invasion of the bronchial glands* and pleurisy may be followed by periods of latency of the tuberculous process but remains a menace.

Tuberculous empyema, unless treated early, may include persisting sinuses and, as mentioned in the chapter on Purulent Pleurisy, may lead

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to amyloid disease. Tuberculous pleurisy does not often lead to empyema when modern methods of treatment are used.

Pneumothorax and pyopneumothorax may result from the breaking of adhesions over cheesy herds or cavities or the separation of an adherent pleura. The significance of this complication is always serious in advanced cases and has been considered in connection with Chronic Pulmonary Tuberculosis.

Retractions and deformities of the chest are not as frequent as formerly, because of early radical treatment and pulmonary gymnastics; in some cases pulmonary fibrosis follows and with bronchiectasis, the patient falls into a condition of chronic invalidism which may continue during many years.

In acute miliary tuberculosis, the pleura may be studded with deposit, a part of the disseminated disease, in which the prognosis is always bad.

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4. Parotid and Thyroid Tuberculosis

The prognosis of tuberculosis of the parotid is good. The disease is usually primary, superficial and amenable to surgical and early treatment.

Tuberculosis of the Thyroid

Tuberculosis of the thyroid is rarely primary, it is usually acute and part of a general miliary infection. In children, with acute infection the thyroid rarely escapes tuberculous deposit. There may be no subjective or objective evidences of thyroid disease.

Secondary nodules isolated in the thyroid may calcify or heal without causing symptoms.

Hector Mackenzie found but one case of Graves's disease in a tubercu-

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lous subject, while on the other hand he cites L. Levy who had "13 cases of Graves's disease among 170 tuberculous patients; such an experience must be quite exceptional." My experience is in accord with Hector Mackenzie, for in a large experience with typical and atypical exophthalmic goiter and tuberculosis, I have rarely found these complicating each other.

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5. Nasal Tuberculosis

Nasal and oral catarrh, non-tuberculous, are frequently annoying and aggravate cough during all stages of pulmonary or laryngeal tuberculosis. The *"dry catarrh"* of the consumptive interferes materially with his comfort, though it is at no time threatening to life.

Ozena opens the avenues to tuberculous infection and may finally become tuberculous.

Single tuberculous ulcers settle by predilection on the cartilaginous septum low down and are amenable to treatment. *Tuberculoma* and *diffuse tuberculous infiltration* of the *nasal mucosa* with final ulceration, may prove destructive, leading to *perforation* and loss of bone.

If the *lesions are limited,* radical treatment will overcome them; if, however, *infiltrating* or *multiple,* single lesions may heal, but relapse and fresh ulcerations are the rule. Naturally the prognosis must depend upon the associated conditions, particularly upon the extent of the primary disease, and the general condition and social status of the patient.

Post nasal, pharyngeal tuberculosis is not prominent during life; there are but a few symptoms which lead to its discovery. The condition is a part of the general infection. *Post mortem* ulcers of the pharynx are not infrequently found. During life their presence has no material bearing on the course of the disease.

6. Laryngeal Tuberculosis

For the purpose of the internist it may be concluded that:

(a) *Primary laryngeal tuberculosis* is exceedingly rare, but is among the possibilities. It may be associated with perichondritis or may limit itself to the mucosa and submucous tissue.

(b) Laryngeal tuberculosis is as a rule a *secondary process.* Its favorite seat is on the anterior surface of the posterior laryngeal wall and the arytenoid cartilages.

(c) Laryngeal tuberculosis shows prompt *tendency to infiltration* of the underlying tissues and to ulceration.

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(d) *Miliary deposit* in the larynx is not exceptional.

(e) Ulcerations may be single or multiple, and *"tuberculous tumors"* (*"tuberculoma"*) may form with associated edema of the glottis.

(f) The tuberculous laryngitis of the *terminal stage* of pulmonary tuberculosis is a potent factor in hastening the end.

(g) Laryngeal tuberculosis with pulmonary phthisis is rapidly *aggravated by pregnancy and childbirth,* and offers an unfavorable prognosis, so bad, that laryngologists have often considered the advisability of inducing abortion to save the life of the mother.

Robert Levy makes the following statement:

"I know of no disease into the prognosis of which so many items enter as into that of laryngeal tuberculosis. The stage of the affection, the nature of the lesion, the situation of the lesion, the complication, the associated general or pulmonary involvement, the environment of the patient, the social position, all and more must enter into a consideration of the possible termination." The spontaneous healing of laryngeal tuberculosis is so rare as to deserve but little consideration in offering a prognosis; a view which most modern laryngologists entertain. At the meeting of the Verein Deutscher Laryngologen in 1911, Dreyfuss, Kummel and Rumpf, held opposite views. Killian contended that these cures were found in those who lived in the open air, the patients had practically received the modern treatment for the primary disease.

Where laryngeal tuberculosis exists with pulmonary consumption, the leading data for prognosis must always be given by the latter, i. e., the primary disease. *Moderate pulmonary invasion* with *limited laryngeal infiltration* or ulceration offers a good prognosis. Fever, anorexia, dysphagia, edema of the glottis, with pulmonary and laryngeal tuberculosis are all unfavorable and hasten the end.

Early recognition of laryngeal tuberculosis and *prompt treatment, local* and *climatic* offer great encouragement. Levy quotes Brüll who "found 58 per cent of his cases clinically cured when they left the sanitorium, and that of these, 31 per cent remained cured."

Men show greater tendency to cure than women, 30 per cent against 26 per cent.

There are many *chronic cases* in which there is, as the result of *local and climatic treatment, cicatricial repair of laryngeal lesions* with resulting *deformity,* consecutive *hoarseness and noisy breathing.* Patients may live many years in this condition. No case of pulmonary tuberculosis is favorably influenced by the advent of laryngeal invasion; the danger is greater when the disease is active; tubercle deposits are numerous and there is ulceration with edematous swelling. With infiltration only, the progress of the lung disease is not materially hastened. I know of no case of cure in my practice in which laryngeal and advanced pulmonary tuberculosis were coincident.

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We ought never to divorce ourselves from the consideration of the influence of *predisposition* and the *social status* of the patient in reaching safe conclusions for prognosis.

Advanced larnygeal lupus offers an unfavorable prognosis; limited infiltration may yield to *radium or mesothorium.*

Tracheal and Bronchial Tuberculosis

Ulceration of the trachea and larger bronchi are usually associated with advanced laryngo-pulmonary tuberculosis, associated with *enlargement and caseation of the bronchial glands,* always (practically) *secondary* and terminal manifestations, in which the end is not long postponed.

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7. Tuberculosis of the Digestive Tract

The Lips.—Labial ulcers are rare; they are occasionally found in the advanced stage of laryngeal or pulmonary tuberculosis, and, barring the pain which they cause, have no bearing on prognosis. When they are present early, the diagnosis may prove difficult without inoculation or bacteriologic tests.

The Tongue.—Tuberculous ulcerations of the tongue may be present with or without lip ulceration. These lesions show characteristic tubercle deposit, and ulceration soon follows with uneven edges, without the "punched out" appearance of the specific ulcer. *Lupus of the tongue and lips* is less likely to ulcerate than is the usual form of tuberculous deposit.

Tuberculosis of the lips, tongue or tonsils, may be either primary or secondary and is usually caused by the human type of tubercle bacillus, though there are occasionally positive evidences of bovine infection. *Tuberculosis of the tongue* with *invasion of the surrounding glands,* often extensive, is not infrequent and is usually a part of a widespread process which is destructive and fatal.

The Tonsils.—The tonsils are important organs in conveying tuberculous disease. They harbor bacilli of tuberculosis, transmit them to the surrounding glands and thus become directly responsible for the dissemination of the disease. During active tuberculosis the tonsils are always found to hold bacilli and often show remnants in chalky deposits of healed tuberculosis. Tonsils may hold tubercle bacilli during long periods without recognizable pathologic change in their structure. There can be no doubt of the fact that the tonsils of children often than adults furnish a

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focus for general tuberculous infection through the cervical lymphatics; these facts have been fully corroborated by Latham and Schlenker.

To prevent descending infection, all *suspected tonsils should be excised early.*

The tonsils are often invaded during pulmonary and general miliary tuberculosis without much enlargement or disagreeable symptoms or ulceration. In occasional cases, where there is marked tendency to breakdown of tissues, small or large ulcers form in the tonsils and soft palate. With laryngeal tuberculosis in the terminal stage of the disease, ulceration, edema and swelling of the tonsils and of the mucosa of the upper air passages add to the discomfort of the dying patient.

The prognosis of *primary tonsillar invasion* is good. With tonsillar and pharyngeal invasion, as with nasal tuberculosis, the larger elements which influence prognosis are the extent of the primary disease, the resistance of the patient and the many other factors to which I have referred in the general consideration of tuberculous disease. It must be remembered that primary, labial or oral tuberculosis may promptly lead to infection of the intestinal and respiratory tract.

The Esophagus.—Esophageal tuberculous ulcers occasionally complicate distant, usually pulmonary or intestinal tuberculosis, offer few or no symptoms, and are usually overlooked during life. If symptoms are present, the general process is usually advanced and the prognosis is correspondingly bad.

The Stomach.—Reference to the *dyspepsias* of tuberculosis has been frequent in considering the subject generally, and their association with the acute and chronic forms of pulmonary tuberculosis. *Intolerant stomachs* are always a source of anxiety, particularly when during the incipient stage of pulmonary tuberculosis all other factors, including environment, are favorable and the patient is handicapped because of the revolting stomach.

True tuberculous lesions are so rarely found in the stomach (tuberculous ulceration, etc.), that they demand no consideration in this work. (See statistics of Melchior, Fredrichs, Dürck, Simmonds, Glaubitt and others in Bandelier and Roepke, 1914, p. 414). *Chronic gastritis,* due to stasis, may add an element of depression during the advanced stages of pulmonary tuberculosis with insufficient heart strength. *Acute gastritis* reduces the strength of the consumptive; it may recur at intervals.

With miliary tuberculosis (general), the stomach is frequently the source of *uncontrollable symptoms; malnutrition* with associated *anemia, high temperatures* often, *rapid pulse,* with advancing evidences later of *intestinal involvement,* lead to death.

In many cases the prognosis is still further influenced by persistent *lack of free hydrochloric acid* in the gastric juice.

Intestinal Tuberculosis (*Tuberculous Enteritis*).—(a) PRIMARY.

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Most primary tuberculous infections of the intestine are found among children and are due to *tuberculous milk, meat,* or contamination of food with *other tuberculous material.* In *primary intestinal tuberculosis* in children there may be no symptoms of pulmonary disease; the child presents the symptoms of acute or subacute gastro-enteritis, the wasting is usually rapid, loss of strength prompt, fever and increasing anemia striking; the weakness is often out of proportion to the diarrhea. *Enlargements of the mesenteric glands* are often palpable as the disease advances. In children there is rarely *intestinal perforation* and there is no tendency toward spontaneous repair. There is in some cases associated tuberculous lymphangitis with deposit of small tubercles on the serosa over the intestinal ulcers. *Primary tuberculosis of the intestine* is associated with greater invasion of the *intestinal glands* than is secondary enteritis, which shows but little tendency to more than slight swelling of the mesenteric glands, *rarely nodules or caseation.* The *prognosis of the primary intestinal tuberculosis* of early life is absolutely bad. The *duration* of life varies from 6 to 8 weeks to as many months after the onset of symptoms.

(b) SECONDARY TUBERCULOUS ENTERITIS is present in all cases of advanced pulmonary tuberculosis, according to Albrecht, in which there is cavity formation. In these cases *isolated* and *characteristic ulcers* are found, or there may be multiple ulcerations throughout the small and large intestines. As already mentioned in connection with the primary tuberculous ulcers, the secondary enteritis is not associated with more than slight enlargement of the mesenteric glands; there are but few or no nodules and there is rarely caseation. There may be *far-reaching intestinal tuberculosis* with but *slight deposit at one or both apices,* which may run a rapid course with all of the symptoms of general infection (Pässler).

Secondary enteritis is probably due to the swallowing of tuberculous sputum. Unquestionably intestinal infection is promptly associated with tubercle bacilli in the lymph of the thoracic duct and the blood of the portal system, and hence leads to flooding of the organism with tubercle bacilli which may have some influence on *immunization* or, what is more probable, causes *metastases* in the already infected lungs and other organs of the body (Fischer). *Intestinal tuberculosis through the blood and lymph stream* causes the deposit of masses of grayish tubercle nodules in the spleen, kidney and adrenals.

Not all ulcers found in tuberculous subjects are tuberculous; some may be due to associated *mixed infection;* the influence on the course of the disease is not materially different, for with the tuberculous as well as pyococcous ulcerations the resulting *colliquative diarrhea* is equally exhausting, and with increasing evidences of depletion, these patients die of exhaustion, enormously emaciated; often there are evidences of amyloid degeneration.

Chronic tuberculous enteritis may follow an early stage of pulmonary

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tuberculosis, when it is due to changes chargeable to toxemia, stasis, atrophy, atony or inflammatory swelling of the mucosa (Bandelier and Roepke). In this class of cases the immediate prognosis is favorable, for these patients may live, comparatively comfortable during many years unless the primary disease makes rapid progress; they may be favorably influenced by diet and climate. Hippocrates' dictum may be accepted as true to-day. "Diarrhea added to consumption is a fatal complication." By this is naturally meant tuberculous enteritis with colliquative diarrhea.

In occasional cases, symptoms of *intestinal stricture* with coiling of intestines, follow tuberculous invasion of the ileo-cecal region, or there may be multiple constrictions due to ulcerations which have followed faulty healing processes. These structures are clinically often mistaken for carcinoma. The neighboring lymphatics are likely to be enlarged and adhesions are not uncommon. They may be either of primary or secondary origin; about $\frac{1}{3}$ are favorably influenced by operation. In some cases the course is chronic.

The Liver.—*Fatty degeneration of liver tissue,* either widespread or limited, is one of the more frequent complications of pulmonary tuberculosis. Liver cells are surcharged with fat, and enlarged. In advanced cases the entire liver may become fatty. As the fat of the body is consumed, the deposit in the liver increases, hence prognostic conclusions are easily reached in the presence of subjective and objective symptoms of fatty liver. Lorentz proved that among the emaciated marasmic tuberculous subjects, 34.8 per cent were found with fatty livers, while this condition was absent among the acute tuberculous infections.

Amyloid degeneration of the liver is always a late manifestation of chronic tuberculosis, is associated with similar change in other organs (spleen, kidney, adrenals, bone, etc.) and with dropsies.

Cirrhosis of the Liver and Tuberculosis.—The examination of the material at the Strassburg Medical Clinic showed 21 cases of tuberculosis among 85 cases of cirrhosis of the liver, 25.5 per cent. Lorentz among 4,337 post mortems found 111 cases of cirrhosis and among these 22 cases of tuberculosis. Among 59 cases of cirrhosis as the leading cause of symptoms there were 6 cases of tuberculosis, and, in 52 cases of cirrhosis considered incidental, tuberculosis was the primary disease among 16.

It is positive that *cirrhosis of the liver invites tuberculous disease;* on the other hand it may be concluded with certainty that primary tuberculosis does not often lead to interstitial hepatitis (cirrhosis). Widespread or limited tuberculosis in the presence of advanced cirrhosis of the liver may be safely considered to have followed and not preceded the latter disease.

The statistics (Bandelier and Roepke) prove the incidence of tuberculosis with cirrhosis in 20 per cent of cases, while cirrhosis following tuberculosis is found among less than 2 per cent of the former. Rolles-

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ton states that in 706 fatal cases of cirrhosis collected from literature, 209 (or 29.6 per cent) presented some evidence of tubercle; (the general incidence of tuberculosis in deaths from non-tuberculous disease is only about 13.5 per cent). Tuberculous lesions were found in the lungs of 22.6 per cent of a series of 584 cases of cirrhosis. Pulmonary tuberculosis is the direct cause of death in from 12 (Kelynack) to 14.5 (Rolleston and Fenton) per cent of patients with cirrhosis. In 9 per cent of the series of 584 cases there was peritoneal tuberculosis. As to cirrhosis following tuberculosis, Rolleston believes that "there is no reason to think that genuine cirrhosis of clinical importance is primarily produced in this way."

Cirrhosis with tuberculosis runs *a rapid course* with marked ascites, usually hemorrhagic. Pain and tenderness are slight as is jaundice also. Pleural effusion, usually double, adds to the suffering of the patient and hurries the end.

Primary tubercle nodule in the liver is exceedingly rare; usually found post mortem. If palpable and large it may simulate carcinoma. F. Krause reports a unique case of a man, age 33, which he operated successfully for primary tubercle of the liver in which the original diagnosis was uncertain; both cancer of the liver and transverse colon had been suspected. Microscopic and bacteriologic examination proved the growth to be tuberculous. There was prompt and uneventful return to health. Pertik in 1904 found but 19 similar cases in medical literature. Orth reports two cases in both of which he was thoroughly convinced that the growths were primary; in the first tuberculous peritonitis finally developed. With *miliary tuberculous generally disseminated,* the multiple deposits in the liver are simply a part of a general process which usually leads to death.

With advanced *chronic ulcerative pulmonary tuberculosis* the liver may hold several large caseous nodules; often there are nodules in the spleen at the same time, while the intestinal glands are ulcerated and the intestines are involved. With such lesions death is not long postponed. With *acute tuberculosis* the enormous bacillemia naturally leads to liver tuberculosis, though the liver function unquestionably tends to destroy tubercle bacilli and other bacteria brought to it through the blood stream and thus prevent its own tuberculization.

Tuberculous perihepatitis complicates *tuberculous peritonitis* frequently, but adds little to its seriousness.

The prognosis of all forms of liver tuberculosis must be considered to be serious, for it may almost always be assumed to be a part of a widespread and progressive process.

The Gall-Bladder.—The gall-bladder may be the seat of primary tuberculosis with other ulcerative and chronic processes, or the bladder and bile passages may become tuberculous in association with pulmonary, peritoneal, acute general miliary, or the tuberculous invasion of any of the

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abdominal organs. *Primary tuberculosis of the gall-bladder* offers a good prognosis when operated early; naturally the diagnosis will as a rule be made by accident only.

Ischio-rectal tuberculosis has already been mentioned and I must repeat that when an early complication of any form of distant tuberculosis, its radical treatment can have only a salutary effect. The persistence of the discharge is always a weakening drain. Superficial treatment without the removal of the tuberculous, i. e., fistulous tract, is useless. I have never known in my experience of the exacerbation of lung symptoms after the cure by operation of tuberculosis of the ischio-rectal fossa. Ischio-rectal abscess is often an evidence of primary and local tuberculosis (Elsner), and offers an excellent prognosis when radically treated. Such treatment will often prove life saving, for in the predisposed the ischio-rectal fossa is a favorite seat of primary tuberculous disease.

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8. Tuberculous Peritonitis

The dictum of Louis (1825) that *chronic peritonitis* is usually of *tuberculous origin* has been accepted by the profession. Tuberculous peritonitis may be—

(a) Miliary peritoneal tuberculosis.
(b) Chronic tuberculous peritonitis.
(c) Chronic fibroid tuberculous peritonitis.

It is difficult in the individual case to reach positive conclusions concerning the focus from which the peritoneal disease spreads. A large number of cases will always remain problematic. It is safest for our purposes to conclude that in the larger number of cases the disease spreads from a preëxisting deposit; that in over *50 per cent of cases* in women it is a part of genital tuberculosis; that the spread from the Fallopian tubes is most frequent; that in children the intestines may supply the infection; that tubercle bacilli may pass through the intestinal wall to the perito-

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neum; that there is no form of pulmonary or other tuberculous disease with which secondary peritonitis may not develop; that *the peritoneum may be invaded in a process of multiple tuberculous periserositis with the pleura, pericardium and occasionally the meninges.*

The terminal stage of *chronic cirrhosis* of the liver may be complicated by an active peritoneal tuberculosis. Osler presents his statistics showing the disease twice as frequent in females as in males (131-60) and in 357 cases which he collected 27 were under 10 years:

75	between	10	and	20	years.
87	"	20	"	30	"
71	"	30	"	40	"
61	"	40	"	50	"
19	"	50	"	60	"
4	"	60	"	70	"
2	above 70 years.				

He also found the disease more frequent among blacks than whites in his service at the Johns Hopkins Hospital.

Borschke, in 4,250 autopsies of which 1,393 were tuberculous, found 226, or 16⅛ per cent, in which the peritoneum was involved. These statistics vary in different sections; thus Nothnagel makes the statement that his experience in Vienna proved the peritoneum to be involved oftener than in Germany. The experiences in the United States prove the association of peritoneal with other tuberculous infections in from 10 to 15 per cent of autopsied cases.

(a) Miliary Tuberculosis of the Peritoneum

In these cases there is *hematogenous infection*, far-reaching, deposit of thousands of millet-seed sized tubercles on the peritoneum and on the liver and the spleen, with or without *ascites;* usually the latter is limited and likely to be serofibrinous, bloody or purulent. There may be circumscribed areas of flatness due to *sacculation.* In these cases there are usually, as the disease advances, abundant adhesions, anatomic evidences of perihepatitis and perisplenitis. The disease may progress with *marked wasting and little fever*, or there may be *decided febrile movement, progressive anemia, rapid pulse;* the course is acute and rapid.

When *peritoneal tuberculosis* is a part of a *general infection*, the local symptoms may be marked or remain unnoticed because of the prominence of the changes in other organs. *Diarrhea, fever and rapid pulse* are occasionally prominent and an unfavorable combination. *Severe pains with circumscribed areas of dullness* and *evidences of adhesions,* are at times associated with ballooning of the intestines, evidences of partial constriction, *chronic obstipation, alternation of constipation and diarrhea, with progressive loss of strength and flesh.* This complex presents factors which

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influence prognosis unfavorably. *The greater the ascites with miliary deposit, the better is the prognosis; this conclusion may be accepted without hesitation.*

Peritoneal miliary tuberculosis, a part of a general tuberculosis, *with vomiting, pain* and *tympany* is always serious and offers a bad prognosis. *Miliary tuberculosis limited to the cecum, simulating acute appendicitis,* when promptly treated, offers a fair prognosis during the active years of life. *Cases beginning with symptoms of enteric fever, without marked lung invasion,* with occasional *rigors,* sometimes a remittent type of fever with slight ascites, when recognized early and radically treated, offer a fairly good prognosis.

Ascites *in children with acute abdominal symptoms is always suggestive of acute peritoneal tuberculosis;* these cases are easily diagnosticated and their progress is usually favorable, if radically treated.

My experience with the disseminated and mixed forms of peritoneal tuberculosis in children, caseous, glandular deposit and miliary disease, has been unusually favorable. I number among those perfectly cured and grown to manhood a good number, in whom, during early childhood, at the time of operation, the disease was so extensive as to justify only the gloomiest forecast.

The prognosis of miliary tuberculous peritonitis is much better in children than in the adult.

Positive evidence of *active tuberculosis elsewhere than in the abdomen* reduces the chances of recovery. The more acute the onset the more unfavorable the prognosis. Murphy disagrees with this conclusion. Rolleston calls attention to *purpura* (cutaneous hemorrhages) and *diarrhea* as "very grave indications." *Non-febrile cases* in adults with *negative tuberculin reactions* have in my experience been uniformly fatal.

(b) Chronic Tuberculous Peritonitis

(Caseating and Ulcerative)

I have been encouraged to believe that cases which give prompt tuberculin reactions (cutaneous and subcutaneous) offer a correspondingly good prognosis. The *fewer associated complications* present, the better is the prognosis. The *greater the ascites,* the better the prognosis; bad when *hemorrhagic or purulent.* The *less the diarrhea* the more favorable is the outlook. *Associated Addison's symptom complex* (suprarenal disease) adds decidedly to the dangers and reduces the chances of recovery.

Mixed infection, causing fever, night sweats, an unfavorable blood picture (Arenth "Verschiebung") and marked leukocytosis argue against recovery. *Favorable environment* is a decided factor in preventing relapse after latency or apparent cure. The future of the patient depends

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very largely on the social conditions which prevail, for with peritoneal this is as important as with pulmonary tuberculosis.

(c) Chronic Fibroid Tuberculous Peritonitis

Many of these cases offer but few symptoms, run a chronic course covering many years, during which the patient remains *in statu quo*, without ascites but with many adhesions and considerable thickening. The majority of cases run their course without ascites; the disease may be subacute or it may prove to be the final stage of an acute miliary tuberculosis. A small proportion of cases develop intestinal symptoms; there may be moderate ascites, adhesions and succulation, evidences of partial intestinal obstruction from bands; the disease may remain afebrile during long periods; chronic invalidism with indefinite symptoms is not unusual.

In occasional cases the retrograde process begins with acute exacerbation of symptoms, fever, increase of abdominal tension, ascites and emaciation. The number and extent of adhesions necessarily influence the course of the disease. It is surprising to note the extent of the disease at the time of operation and the favorable results which often follow. This agreeable experience may be found with complicating chronic tuberculous pericarditis and pleuritis. In the presence of nodular deposits and fibroid peritoneal thickening, it is not always easy to decide whether the process is tuberculous, a fact to which Welch, Wood and Fitz, and Henoch have called attention and deserves consideration in offering prognoses. In these cases the peritoneum is studded with nodular growths; there are associated inflammatory exudates, usually serous, in which the prognosis is most encouraging.

Surgical Treatment and Prognosis

The influence of *radical treatment* (operative) on the prognosis of tuberculous peritonitis is of the greatest interest and importance. The study of a large clinical material has led me to the advocacy of early surgical interference in all cases of tuberculous peritonitis in which complications offer no contra-indications, with encouraging results—recovery in 80 per cent of such cases. The English authorities argue against operation in infants under 12 months. I number among my cases a lad now 20 years of age who was but 10 months of age at the time of operation, with large multiple tubercle nodules in the abdomen, succulated serous effusion and adhesions, who has continued in perfect health and shows no lesions at present.

The prognosis is unfavorable after surgical interference in the presence of *general and widespread tuberculosis.*

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The most favorable results follow operation for chronic tuberculosis of the peritoneum with ascites, and some surgeons are now limiting their surgical treatment of peritoneal tuberculosis to that class of cases. Schramm reports with children 80 per cent of cures among the operated and 64 per cent among non-operated cases. Pic admits recoveries among 74 per cent of the operated against only 5 per cent of the non-operated cases. Sutherland makes the startling statement that he found 50 per cent of recoveries among the operated and 81 per cent of recoveries among non-operated cases. Thus Rolleston submits the result of his experience in cases gathered from literature and practice as follows: Of 125 cases treated by operation there were 88 recoveries, 70.4 per cent; of 156 cases not operated there were 51 cures, 33 per cent.

My experiences justify the conclusions that in carefully selected cases, without barring young children, basing such selection on data furnished in the preceding paragraphs of this chapter dealing with tuberculous peritonitis, the prognosis is enormously improved by early conservative surgical treatment. Further, while the disease may heal spontaneously, such incidence is not of sufficiently frequent occurrence to be depended upon in the majority of cases "spontaneous cures" are not always lasting; periods of latency are not infrequent and among spontaneous cures and latent peritoneal tuberculosis there are many recurrences, more by far than follow after operation; the dangers of dissemination are also greater among the apparently cured without operation than among those who have been helped by surgical methods. My experiences further agree very closely with those of Bandelier and Roepke that 96 per cent of untreated tuberculous peritonitides die; of these 50 per cent die in from 1 to 6 months, 25 per cent in from ½ to 1 year; the remaining cases may live with persisting symptoms during long periods, the length of time depending on many factors previously considered.

My clinical material includes but two cases in which the operation was followed within a few days by the death of the patient. In one, the patient a boy age 18 seemed to present conditions that were favorable, his temperature had been high, the pulse rapid and small, there was abundant ascites, without evidences of distant tuberculosis in physical signs, but the acute history justified the strong suspicion of general miliary tuberculosis. The operation was followed by continuous hyperpyrexia during three days and the death of the patient. There was far-reaching miliary disease. The second case was practically a repetition of the first, with prompt lethal ending within seven days.

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9. Tuberculosis of the Pancreas

Tuberculosis of the pancreas is so rare as to be of slight clinical or prognostic importance. If found, it is in children with generalized tuberculosis, and is without marked influence on the progress of the disease. Pitt reports one pancreas tuberculous in 2,000 autopsies and accounting for ½ per cent "of all cases in which pancreatic disease has been noted."

Mayo and Sendler have successfully removed tuberculous masses from the pancreas or from the neighboring lymphatic glands which were palpable.

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10. Tuberculosis of the Spleen

In all forms of *disseminated tuberculosis, tuberculous deposits* varying in size are found in the spleen. In some cases the *capsule* is more involved than the spleen itself and there may be consecutive *perisplenitis* and *local peritonitis. Caseation of tubercle* in the spleen with general tuberculosis is possible.

With *chronic pulmonary tuberculosis, multiple tubercles* of considerable size may be present in the spleen, causing enlargement, but no recognizable subjective symptoms. The tubercle grows more rapidly in the spleen than in the liver and is most likely to be found with tuberculosis of early life.

There are cases of *primary splenic tuberculosis* which cause great enlargement of the organ, *polycythemia,* with positive reaction to tuberculin tests, in which splenectomy offers the only hope (over 80 per cent recover if operated early). Tuberculosis of the spleen should be suspected in all cases in which the *organ is enlarged* and in which there is *polycythemia,* without other convincing data. This combination always suggests tuberculin injection or other tests to establish an early diagnosis.

The *prognosis of primary tuberculosis* of the spleen, if diagnosticated early, is favorable with rational surgical treatment.

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11. Suprarenal Tuberculosis—Addison's Disease

(*Suprarenal Tuberculosis, Bronzed Skin Disease*)

The complex of symptoms known as *Addison's disease* is due to destructive disease of the suprarenal glands; one or both are almost always tuberculous. The leading features are: increasing *weakness and asthenia, pigmentation of the skin and mucous membrane of the mouth* particularly, *gastro-intestinal disturbances,* increasing *cachexia, small rapid pulse, low blood pressure, and marked emaciation.* The tuberculous process in the suprarenals is usually bilateral and deposits in distant parts of the body are not unusual.

Elsasser found in 549 cases which he studied 17 per cent with isolated suprarenal tuberculosis; in 43 per cent associated pulmonary tuberculosis; in the remaining cases there were tuberculous herds in other organs. There are cases of *hypernephroma* associated with Addison's complex reported by Bittorf. In 561 cases of Addison's disease the suprarenals were normal in 12 per cent, tuberculous in 75 per cent (Levin).

The description of the disease originally given by Thomas Addison in 1855 ("On the Effects of Disease of the Supra-renal Bodies," London, 1855) remains a classic in medical literature. *Acute infection of the glands* leads to a train of symptoms, without marked pigmentation, but with enormous asthenia, heart weakness, hypotension, depression, melancholia, at times delirium, rapid wasting of fat and muscle and death within from seven to fourteen days. The picture of extreme weakness is strikingly suggestive, coma or other profound nervous and toxic symptoms are soon followed by the end.

In occasional cases there may be vascular changes with or without tuberculosis, thrombosis or hemorrhage into the gland substance, which are responsible for the rapidly fatal termination. *Unfavorable symptoms* are rapid wasting of tissues (faulty metabolism), subnormal temperature, persistent hypotension, diarrhea, marked blood changes, reduced hemoglobin and lowering of red blood count with marked large mononuclear lymphocytosis. *Hypoglycemia,* large grape sugar tolerance and adrenalinemia are also unfavorable. Subnormal temperature followed by marked pyrexia, repeated at short intervals, are exceedingly weakening and depressing and presage an early termination. Failure to produce glycosuria by the liberal injection of adrenalin with other positive symptoms must be interpreted as an unfavorable feature. *Acute cases* show but little or no *pigmentation* as a rule.

The prognosis is better, so far as length of life is concerned, in proportion to the exent of the *pigment deposit.* The more chronic cases show the greatest pigmentation.

Straub reports a most interesting experience with a rapidly fatal acute case of suprarenal disease in which the postmortem showed thrombosis

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of both suprarenal veins, and in which the symptoms of Addison's disease immediately developed including, after a short period of redness of the skin, characteristic bronzing (pigmentation), asthenia, adynamia and psychic disturbance. In this case the blood pressure was but little lowered. *Syphilitic deposit in the suprarenals* may simulate true Addison's disease and may fully recover under treatment. Many reported recoveries were probably of syphilitic origin.

In *chronic suprarenal tuberculosis* there may be periods of latency, remissions, long periods of extreme weakness, during which complications, ordinarily insignificant, are sufficient to cause death. I number among my histories of chronic suprarenal tuberculosis, confirmed by autopsy, one of *associated pernicious anemia* and another case in which there were fully developed symptoms of exophthalmic goiter.

Duration.—There are cases in which, including *periods of latency*, the disease may continue so long as ten years. There is no stage of the disease which may not be complicated by acute exacerbations, which may in turn lead to death within a few days or weeks.

In chronic cases, pigmentation may be an early symptom, preceding during long periods the usual *asthenia* and the pronounced *nervous manifestations* of the fully developed complex. In some of these cases *normal blood pressure* and *hyperglycemia* with *adrenalinemia* may continue during long periods, and are favorable indications. Kraus believes that all cases, if tuberculous, finally develop characteristic symptoms and die.

Typical cases run their course in from two to four years. The development of *mania* or *melancholia* is always unfavorable. *Epileptiform seizures* may precede coma which promptly leads to death. I have never seen recovery from *coma* with suprarenal disease. Kascherininowa at the instigation of von Strumpell has treated a number of cases of suprarenal tuberculosis with tuberculin, with suprisingly good results. Munro has reported similar encouraging results.

There is a class of cases in which, in the last stage of the disease, symptoms resembling *acute peritonitis* develop from which the patient does not recover, but dies in the course of from 3 to 7 days (Ebstein).

I would call the attention of those interested in the literature of suprarenal disease to the additional references at the end of this article.

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12. *Tuberculosis of Lymphatic Glands*

(Scrofula, Scrofulosis, King's Evil)

Cervical Lymphadenitis.—All scrofula is due to the tubercle bacillus and in a large number of cases is purely a surgical and local affection leading to tuberculous adenitis. It is found, as a rule, in children, with the "scrofulous" or "tuberculous habit." The disease by predilection selects the glands of the neck, the bronchial nodes or the mesenterics. There is a *strong tendency toward chronicity* when the *neck glands* are involved, and toward healing, while in most superficial adenitides caseation and suppuration is the fate of the invaded gland. Children who are "scrofulous" are vulnerable. They are "below par," as a rule, though intellectually active. They are prone to recurring phlyctenular conjunctivitis and keratitis, during long periods, bone tuberculosis, ulcerative rhinitis and otitis media; they are easily influenced by *climatic changes* and, as a rule, are not able to endure what is usually expected of the normal child. They are also subject to *skin eruptions* and ulcerations with strong tendency to anemia. The skin over the involved gland breaks down readily and, unless the gland when caseated or suppurating is radically removed, *sinuses and crusting* may persist during many years. *Tuberculous adenitis* provides a focus from which tuberculosis may spread at any time, and it is never safe to harbor such tuberculous deposits.

Bronchial Lymphadenitis.—The invasion of the *bronchial nodes* has been frequently mentioned in connection with the study of tuberculosis and the importance of their prognostic significance has been accented. Pressure of enlarged nodes on veins may prove complicating and cause alarming symptoms in occasional cases. In spite of the fact that tuberculous deposit in the bronchial lymph nodes may often remain latent during many years, there is never a time when such infection is not a menace, and when from it, fatal or active tuberculosis may not be spread. My experiences with these nodes as *provocative of rapidly spreading tuberculous meningitis* have been among the saddest of my professional career.

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Perforation of caseating or suppurating bronchial nodes may cause sudden complications which are rapidly fatal by opening a large vein, an artery, one of the surrounding organs (esophagus, bronchus, lung or pleura), or even the heart sac.

There are cases of *widespread acute tuberculous lymphadenitis* which resemble the *acute form of Hodgkin's disease.* In these cases the patient wastes rapidly with high temperature (102°-106°F.), repeated chills and profuse sweating. The glandular invasion may include the lymphatics of the thorax, abdominal cavity, also the retroperitoneal space and often many superficial glands. Unless we are cautious, these cases may be mistaken for *Ebstein's recurring fever of Hodgkin's disease.* The prognosis is uniformly bad, the course of the disease acute, patients die after a few weeks.

With *active lymphatic tuberculosis* the *blood changes* mentioned in the general consideration of tuberculosis, including pronounced leukocytosis, are present, increased by tuberculin injection with increase of temperature; von Pirquet is positive in infected children with weak dilution.

Mesenteric Tuberculosis (*Tabes mesenterica*).—With tabes mesenterica there is *tuberculosis of the mesenteric and retroperitoneal glands.* Invasion of the glands is most frequent during early life, but there are cases of tuberculosis of the mesenteric glands in the adult, in which the infection spreads from the cecum, only occasionally from the pelvic organs or spine, and in which large masses, nodular and hard, are formed and are easily palpated. These mesenteric enlargements in the adult may remain latent during long periods, may present active symptoms early, with prompt wasting of the patient, may lead to sudden perforative peritonitis, or, with evidences of chronic peritonitis, alternating diarrhea and constipation, lead to death after several weeks or months.

Tabes mesenterica of childhood may be *primary*, but when thorough search is made it will be found that often the enlarged glands are associated with tuberculosis of one or more of the abdominal organs. The association of enlarged mesenterics with acute miliary tuberculosis, peritoneal tuberculosis, intestinal tuberculous ulceration, ileocecal invasion, is not uncommon. It may be assumed that tuberculosis of the mesenteric glands indicates infection by way of the intestines as a rule; that during early life tubercle bacilli easily wander through and beyond the intestinal mucosa without causing the slightest abnormality at the port of entry. The prognosis of all forms of mesenteric tuberculosis is bad. The progressive cases are promptly associated with symptoms which do not keep the attendant in doubt; the wasting is characteristic, the increasing weakness with exhaustion, often diarrhea, rapid heart with small thready pulse, night sweats and fever, later added evidences of peritonitis, with or without ascites, are followed by death. Suppuration is not a frequent sequel. Osler calls attention as do other clinicians to the variation of the statis-

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tics of abdominal tuberculosis in different countries and I quote the following to show these differences. "The small percentage in New York, less than one per cent of all cases (Bovaird and Mt. Sinai Hospital figures), contrasts with the high figure, 18 per cent for England, and the same has been demonstrated recently for Scotland by John Thomson, 3.57 for Edinburgh and 4.51 for Glasgow."

In considering the prognosis of lymphatic and intestinal tuberculosis we must once more call attention to the *theory of von Behring*, which is still *sub judice*, that the intestines ultimately serve as the foci from which pulmonary and distant infection take their origin. For the clinician who may or may not subscribe to this theory, the important fact must always remain, that *in the presence of tuberculosis of the intestinal or mesenteric glands, the dangers of general infection with lung involvement are enormously increased.*

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13. Genito-urinary Tuberculosis

Pathologic and clinical data accumulated during recent years have entirely revolutionized our ideas concerning the prognosis and the manner of extension of genito-urinary tuberculosis. The profession is fast becoming convinced that most forms of genito-urinary tuberculosis are surgical affections.

In no field of medicine have the newer methods made the early localization of lesions more positive than in the urinary tract. I refer more particularly to cystoscopy, catheterization of the ureters, with the tests which give information concerning the funtionating ability of the separate kidneys.

There are four leading facts which influence the prognosis of genito-urinary tuberculosis powerfully, well established by clinical, pathological and surgical experiences. They are:

(a) *The kidney is primarily affected* and but one kidney is at first involved in most cases.

(b) *If there is positive thickening of a ureter* there is coëxistent disease of the kidney.

(c) *Bladder tuberculosis is not primary;* "it is merely scalded and, as such, its irritability is the sentient expression of a suffering kidney." "This, then, is the psychological moment to interfere on the chance of cure." (E. Harry Fenwick.) In other words, bladder tuberculosis is usually secondary.

(d) *Genito-urinary tuberculosis spreads downward* following along the course of the infected urine "with the stream" from kidney to its pelvis, ureter and bladder, not in the opposite direction "against the stream."

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These conclusions, accepted as they are by leading urologists and pathologists and by those who have worked in the field of experimental medicine, are hard to controvert. On the other hand, we cannot deny the force of clinical evidence and the results of experiments, by Wildbolz, Eckehorn and others, which do not entirely justify the exclusion of the spread of genito-urinary tuberculosis from a focus below the kidney, ascending, therefore, not often but with sufficient frequency, to conclude that deposits of tubercle in the prostate, testicle, bladder or anywhere in the tract may spread the infection. Interference with urinary drainage is the leading cause of ascending infection of the genito-urinary tract.

Tuberculosis of the Kidney

Potent factors which influence renal and genito-urinary tuberculosis unfavorably, are the facts, (a) that the disease may exist, make progress, advancing rapidly, without causing subjective symptoms sufficient to create a suspicion of its presence. In one of my cases a man, age 35, died suddenly without evidences of preëxisting disease in symptoms; at the autopsy there was bilateral invasion of the genito-urinary tract, no remnant of normal kidney was found.

(b) From an early stage a large part of one kidney may be involved and in occasional cases the process promptly becomes bilateral (30 per cent).

(c) Changed kidney function may in occasional cases lead to grave constitutional disturbances, toxemia, etc.

(d) In some cases the *bladder* is promptly involved in an ulcerative process, adding to the sufferings of the patient. *Mixed infection* also adds an element of danger which is often overcome with great difficulty.

(e) In occasional cases the *functional activity* of the kidney *is enormously reduced*, as can be established by ureteral catheterization and functional tests; tubercle bacilli swarm in the pus-laden urine, urea is reduced, and there may be grave constitutional disturbance. Gould has called attention to the important prognostic fact that with the presence of tubercle bacilli in a urine "which contains a proper proportion of urea and is free from pus," surgical interference is justified and, after a thorough search of my records and a study of the literature on this subject, I conclude that under these conditions the prognosis may be considered good.

Kidney tuberculosis associated with miliary infection is without marked influence on the general course of the disease which even without the added kidney complication leads to death within a limited time. The type of kidney tuberculosis which the clinician usually meets is the *caseating* and *ulcerative form* in which the first evidences of existing disease are referable to the pelvis of the kidney and are established by urinary examination. The symptoms are those of *pyelitis. To reach safe*

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and early conclusions for diagnosis and prognosis every case of pyelitis in which no positive pathologic cause can be established at once, should create a strong suspicion of renal tuberculosis, and the case kept under observation until this conclusion is corroborated or upset by scientific investigation.

Early hematuria, without other leading symptoms, is often favorable, for it creates in active adults during the years of sexual activity (when genito-urinary tuberculosis is most frequent) the first suspicion of existing tuberculosis, making prompt treatment possible and cure likely. It is a primary symptom in 6 per cent of all cases and is present in 60 per cent during the existence of the disease, oftener in men than in women (Braasch).

The presence of *bladder invasion* does not argue against the possibility of complete recovery. Unexplained bladder irritation must always lead to the suspicion of kidney tuberculosis; it is present in 86 per cent of all cases (Braasch). Its significance, recognized early, will do much to reduce the mortality and improve the prognosis of genito-urinary tuberculosis.

Spontaneous cure or *surgical removal of the primary focus in the kidney*, when the disease is not widespread, as a rule results in the cicatrization or cure of vesical tuberculosis. When kidney tuberculosis is limited to one organ, the bladder and lower end of the corresponding ureter are uninvolved; there are but few or no constitutional disturbances; early recognition and treatment lead to cure in the majority of cases.

The most important question which interests the clinician is:

Is the disease limited to one kidney? In 30 per cent of cases the disease is bi-lateral early. It occasionally happens that the disease is active in one kidney and that a small latent deposit exists in the opposite kidney which escapes detection. With modern methods of diagnosis the chances of diagnostic failure are enormously reduced, though they will occur.

I have seen cases with advanced tuberculosis in one kidney and but slight evidences of disease in the opposite organ, in which the removal of the active focus led to latency and to years of comfort, and occasionally to apparent cure.

Perinephric abscess of tuberculous origin, caused probably through lymphatic invasion rather than perforation of the capsule of the infected kidney, may be an early complication of limited renal tuberculosis; its prognosis is not unfavorable, if the primary focus can be radically treated.

Kidney tuberculosis of limited extent under favorable surroundings may occasionally undergo *spontaneous cure;* if this possibility suffices for the basis of treatment, the majority of genito-urinary tuberculoses will promptly follow their natural tendency toward progression and death.

With advanced pulmonary tuberculosis and disseminated genitouri-

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nary tuberculosis the prognosis is absolutely bad. In 6 to 10 per cent of genito-urinary tuberculosis there is *lung involvement.* Limited lung infection does not argue against the radical treatment of renal tuberculosis; many such cases recover. The conclusions given by Braasch who has scientifically studied the material at the Mayo Clinic, in his "Observations of 203 Patients Operated for Renal Tuberculosis," may be accepted as expressing the most advanced ideas concerning the prognosis and the incidence of the disease. Of the 203 patients operated, 6 died—2.9 per cent. Seventy per cent of the patients were followed during a sufficient time to allow profitable conclusions. Eighteen per cent were dead; of these 60 per cent died before the end of the first year, and 15 per cent lived more than 3 years. Of the 82 per cent alive, all but 13 per cent reported improvement or recovery from their bladder symptoms; their weight and strength had increased materially. Five patients had double infections; all of these died within one year of the operation. Braasch concludes that 75 per cent of renal tuberculosis is curable by the modern methods of treatment, while 90 per cent is fatal without it.

Loss of weight and strength in young subjects with fever and bladder ulceration presents an unfavorable outlook.

In 60 per cent of the Braasch cases of renal tuberculosis in the male, there was deposit either in the epididymis, the testicle, vas deferens or prostate, oftener in the epididymis.

I have occasionally found that an inflammatory deposit left by gonorrheal epididymitis became tuberculous; the prognosis of such cases is good. In one-third of all renal tuberculosis in the male the *prostate* is also invaded. *General infection* may be present with renal tuberculosis and recovery may follow. The prognosis is less favorable when the kidney deposit with breakdown of tissue has advanced sufficient to make the organ palpable. *Kidney tumor* is present in from 20 to 25 per cent of cases.

Persistent fever with symptoms of genito-urinary tuberculosis and rapid small pulse, with increasing anemia and loss of weight are all unfavorable.

Besides the convincing statistics of Braasch to encourage the early recognition of genito-urinary, more particularly, renal tuberculosis, we find Bandelier and Roepke average recoveries after radical treatment at 50 per cent, Israel 63 per cent and Caspar reports 67 cases with 50 cures.

Pregnancy and childbirth usually stimulate renal and genito-urinary tuberculosis to renewed activity. Israel has demonstrated the evil effects of pregnancy in a large number of cases on existing renal tuberculosis. In almost all of these cases rational surgical treatment has proved efficacious.

Blood Pressure.—As in all forms of tuberculosis, so with advanced genito-urinary involvement and kidney degeneration, the *systolic blood*

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pressure will be found below normal; decided *hypotension* is unfavorable and is usually found with a small and rapid pulse, disseminated disease, and advanced ulceration in the terminal stage of the disease. *Progressive fall of blood pressure* with loss of weight is always unfavorable. Failure to improve the circulatory condition by operation is also ominous. The *dangers of secondary invasion* of the meninges, lung, intestines, peritoneum and bone, and the possibility of rapidly advancing amyloid degeneration are not to be ignored in prognosis.

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Genital Tuberculosis in the Female

Menstrual Irregularities.—In the female we find with tuberculosis, *menstrual irregularities* which are usually associated with *chlorotic and anemic conditions.*

The most frequent anomaly is *amenorrhea,* which is often an expression of reduced vitality and may yield as the general condition of the patient is lifted and the blood picture is improved. Amenorrhea with incipient pulmonary tuberculosis without evidences of toxemia or advanced lung change, with *chlor-anemia,* almost always disappears under favorable surroundings unless the disease is progressive. There is in some cases, when advanced, *atrophy of the uterus* to which the amenorrhea has been attributed by Thorn and others. Serious tuberculous diseases of the genital tract in women lead to anemia, particularly when there has been profuse hemorrhage or suppuration; under such conditions there may be amenorrhea or other menstrual irregularities.

The Blood.—The blood condition offers valuable data for prognosis with *genital tuberculosis or menstrual anomalies.*

The following blood picture may be considered unfavorable in the presence of genital tuberculosis:

(a) Marked reduction of erythrocytes and morphologic change.

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(b) Reduced hemoglobin.
(c) Lymphocytosis (34 per cent). Excess of small mononuclear cells.
(d) Prominence of Arenth picture. Displacement to left.

Can Tuberculosis Be Primary in the Female Genital Tract?—Amann makes the unqualified statement that *there is no primary tuberculosis of the genital tract in women.* For our purposes as prognosticians, there are a number of facts which contradict this dictum, though *we must admit its truth in the majority of cases.* Schlimpert is a warm advocate of Amann's contention. The former claims that tuberculoses of the genitals are in 80 per cent of pulmonary origin, in 50 per cent they are secondary to intestinal tuberculosis, and that bone and lymphatic tuberculosis supply the foci for the remaining cases.

The tuberculous diseases of the genitals in women are found in the

I. Fallopian Tubes
II. Ovaries
III. Uterus
IV. Vagina.

When of long duration, the disease is disseminated.

I. **Fallopian Tubes.**—Kermauner claims that the *Fallopian tubes* are involved in from 70-90 per cent of all genito-urinary tuberculosis in women, the uterus in 40-65 per cent and the vagina in 10 per cent. The most patient search in many cases of tubal tuberculosis, fails at the time of the operation to show any other focus, and the large per cent of complete and lasting cures following, argues very strongly against the assumption that these are all of secondary origin. Naturally, the earlier tubal tuberculosis is recognized the better is the prognosis, for the *changes are prompt* and *may progress without subjective symptoms.* Thickening of the tubes with caseation, the formation of creamy and cheesy tubercle bacilli-laden pus, and adhesions are characteristic, and from this focus general peritoneal tuberculosis may advance, or may be aggravated if already existent.

In over 50 per cent of tuberculous peritonitides there is coexistent disease of the Fallopian tubes and ovaries.

II. **Ovarian tuberculosis** is as a rule secondary and is not infrequent; usually the uterus and a Fallopian tube or the latter and the ovary are involved. *Perioöphoritis* is a part of tuberculous peritonitis. The ovarian disease is usually double; one ovary may be more involved than the other. The disease advances in the ovary without materially interfering with the general condition of the patient in chronic cases, with the deposit of either multiple small foci or one or more large cheesy deposits. *Tuberculous salpingitis* may be far advanced without ovarian involvement. *Ovarian and tubal infection* often follow latent, unrecognized, or active general or localized peritoneal tuberculosis. *Unrecog-*

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nized pulmonary deposit, or a *tuberculous focus in some distant organ,* may through the *blood stream* lead to genital infection.

III. **The Uterus.**—When the uterus is tuberculous, the disease is usually advanced in the tubes, in the ovaries, and there are likely to be evidences of adhesive tuberculous peritonitis, matting the pelvic organs together by dense adhesions. *Uterine tuberculosis* leads to cheesy degeneration of the endometrium, which, if neglected, finally invades the musculature, limiting itself as a rule to the corpus uteri. In some cases the patient's condition is reduced by the continuous discharge due to an accompanying *tuberculous endometritis.* (Pyometra tuberculosa.)

In considering the *direction in which genital tuberculosis spreads* (an important prognostic element), it will be found that extension is descending under average conditions, rarely ascending. Baumgarten believes as the result of experimentation that in women the spread of tuberculosis is always in the direction of the wandering of the ovum, while in man the flow of the spermatic fluid marks the direction in which the disease spreads from a primary focus. The unqualified acceptance of this theory is not justified; it unquestionably has exceptions which must be considered by the clinician.

Direct infection of the genitalia in women from without is possible; bacilli may be introduced with the spermatic fluid or in other mechanical ways.

IV. **The Vagina.**—Vaginal ulcers of tuberculous origin may be primary and yield to radical treatment. In advanced genital tuberculosis there may be marked change in the vaginal wall, which, barring the discomfort and pain, does not materially influence the prognosis of the existing primary disease. It is surprising to note how favorably even advanced genital tuberculosis with vaginal invasion is often influenced by thorough treatment.

In all forms of genital tuberculosis there is a strong tendency to the formation of *protective adhesions; nature seeks to hold the disease within narrow limits.*

It occasionally happens that for some unknown reason *general miliary tuberculosis* promptly follows the removal by operation of tuberculous genitalia; this is a rare sequel.

Generally speaking, it may be said that the prognosis of the genital tuberculosis of women is good; that the larger number of cases are accidentally discovered in tubes, ovaries and uterus, though often strongly suspected, that in accordance with modern pathologic views "genital tuberculosis in the male and in the female is not dependent for its origin upon urinary tuberculosis." The safest conclusion for the practical physician to reach is that in the larger proportion of cases *genital tuberculosis is secondary* to a focus for which search should be made, but which may not be found; that the prognosis is so uniformly favorable in such a

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large number of cases that, in at least a number of these, *primary infection must be acknowledged.*

The coëxistence of urinary and genital tuberculosis in both male and female does not of necessity lead to death; there are many cases which are favorably influenced by surgical and medical treatment, while in some there may be spontaneous cure, or long periods of latency are established. Without an appreciation of the dangers of coëxisting genital and urinary tuberculosis and rigorous treatment to establish resistance, the prognosis is grave.

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14. Cardiovascular Tuberculosis

Reference has frequently been made to the heart, its small size, the involvement of the myocardium, and to the possibility of spreading miliary tuberculosis from the infected blood vessels, and the prognostic significance of cardio-vascular invasion. The statistics of Weigert proved 50 per cent of all miliary tuberculosis traceable directly to vascular tuberculosis, while to-day statistics (Schmorl, Lubarsch, Benda) prove 95 per cent of all miliary tuberculosis to be dependent upon this method of dissemination. Hence, every local tuberculous herd, closely related to an artery, vein, or thoracic duct, or the lymphatic stream, remains an element of danger. *Vascular tuberculosis or infection represents therefore, the link between the primary focus and miliary tuberculosis, a dictum of enormous prophylactic and prognostic value.*

Tuberculosis of the Aorta.—Tuberculosis of the aorta and other vessels may develop and lead to death. In these cases bacteria "penetrate the inner lining of vessels from the main channel," in the presence of a forcible blood current, causing inflammatory change of the intima and *secondary thrombosis.* (Flexner, Blumer, Stroebe, Aschoff, Schmorl, Krumbhaar, Hekton).

Tuberculous Pericarditis.—Tuberculous pericarditis is rarely primary; it is usually part of a widespread process (pleural, pulmonary, lymphatic) which may run a chronic or an acute course. In chronic cases adhesive pericarditis may lead to stasis, edema, dyspnea, anginoid attacks, evidences of abdominal dropsy with enlarged liver and spleen, and cyanosed kidney.

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The *acute cases* often lead to *hydropericardium,* which may be hemorrhagic with preponderance of lymphocytes (50 per cent and more) in the fluid.

While the prognosis of tuberculous pericariditis is supposed to be *unfavorable,* we have found in practice that occasionally latency and cure may follow, and that, with disseminated tuberculosis, peritoneal and pleural, with but little or no lung invasion, cases have been cured by radical surgical interferences. We number among our medical colleagues one such fortunate case in which there was widespread tuberculosis of the pleura, peritoneum and pericardium, in which after eleven operations, including one pericardial resection (cardiolysis of Brauer) and relief of adhesions thereby, there is now complete recovery, with sufficient strength for the patient to resume practice. Romberg reports 16 cases of tuberculous pericarditis of which only four died, while 4 of his 10 idiopathic pericarditides died.

Myocardium.—With miliary tuberculosis there may be deposits in the myocardium; these offer no symptoms which prove their presence, and as Romberg has said, "interest the pathologist more than the clinician."

The change which is almost constant with tuberculosis is *fatty degeneration of the myocardium* with marked anemia in the terminal stage of the disease. *Tuberculous deposits in the myocardium* in chronic phthisis are exceedingly rare. Willigk found but two hearts in which there was tuberculous deposit in 1,845 tuberculous subjects autopsied by him.

Endocarditis.—Endocarditis of purely tuberculous origin is also rare. Occasionally there are a few vegetations on the endocardium with characteristic histologic build. But, as Marshall has demonstrated, the incident is not of sufficient frequency to justify the suspicion of its presence; on the other hand, when present, no symptoms make its recognition positive. Michaelis and Blum have proved the possibility of producing tuberculous endocarditis experimentally.

Not all valvular lesions found in the tuberculous subject are due to the tubercle bacillus. Many of these lesions are old and of rheumatic (streptococcus rheumaticus) origin.

In early life endocarditis tuberculosa may develop with general miliary tuberculosis. All of these children die. In the adult, *endocarditis due to streptococcus infection* may complicate tuberculosis or there may be *chronic ulcerative endocarditis* with tuberculosis, in which the Streptococcus viridans has proved to be the pathogenic factor. This complication may hasten the progress of the primary disease, but runs a chronic course, being the cause of most chronic malignant endocarditis. Klebs has also reported acute mycotic endocarditis with tuberculous phthisis.

Thrombosis.—The formation of heart clots, thrombi in the pulmonary artery or veins of the body—ante mortem—in tuberculous sub-

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jects, is a cause of death which was recognized by Rokitansky, Klebs, Birch-Hirschfeld, Weichselbaum and others. In these cases, depending on the location and extent, there may be gradually increasing symptoms during several days or death may be sudden. *Peripheral venous thrombosis* in the terminal stages of phthisis is frequent. Dodwell found the proportion of cases with this complication to be about 3 per cent. These peripheral thromboses are found in the terminal stages of the disease, when the circulation has become insufficient.

Constriction of Veins.—Constriction of veins—one or more—by new connective tissue, causing *blowing systolic murmurs* in various parts of the lung, may appear alarming to the inexperienced; as a rule, they add but little to existing dangers.

Pulse.—Changes in *frequency* and *rhythm* of the pulse often offer valuable prognostic data. The tachycardia of the end stage, during which the pulse may reach 200 per minute, is always of great prognostic importance; with such a pulse, sudden cyanosis and death may follow.

The Heart.—Whatever conclusions we reach concerning the *size of the heart in the tuberculous subject,* we must admit that Brehmer's contentions (that the heart is undersized; that unless aided by proper methods it sends insufficient blood to the lung; that, as the direct result of its congenital fault, it is largely responsible for the development of pulmonary tuberculosis) have, with the impetus received by the approval of Dettweiler, lead to the most rational and successful therapy of tuberculosis, the basis of which is the improvement of the tone of the insufficient heart, and all muscles, and the upbuilding of the patient. The theory of Rokitansky already mentioned in the general consideration of tuberculosis, that *heart lesions antagonize* pulmonary tuberculosis, particularly those which produced venous stasis (initial lesions particularly) has been considerably shaken during the past fifty years. Fromholz found in 7870 autopsies, 277 valvular lesions (3.5 per cent) of which 22 (8 per cent) had pulmonary tuberculosis. With but one exception these were associated with disease of the left heart. *Mitral stenosis* certainly antagonizes the development of tuberculosis of the lung as does *mitral insufficiency* with marked pulmonary engorgement and *brown induration* of the lungs.

Blood Pressure.—I have already referred to the behavior of the blood pressure in pulmonary tuberculosis. Its progressive fall with small pulse is always unfavorable. Rise of blood pressure with even slight gain of weight is favorable, for it is suggestive of control of the process.

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15. *Tuberculosis of the Nervous System*

Tuberculous Meningitis.—The prognosis of tuberculous meningitis is considered in connection with miliary tuberculosis. (See Miliary Tuberculosis.) Single tubercle nodules may exist in the brain without giving rise to symptoms or there may be positive evidences in symptoms of *tumor of the brain.* In another class of cases there may be sufficient improvement to justify the conclusion that the patient has made a fair recovery; periods of latency are not unusual, followed by sudden exacerbation and death; or spontaneous cure due to encapsulation or calcification, if the masses are small, may be followed by entire freedom from symptoms.

Spinal meningitis, leptomeningitis, of primary origin is so rare as not to require consideration. When the pia is invaded, it is part of a disseminated process, whether miliary, i. e., multiple deposit, or single large cheesy tubercle, with possible involvement of the cord, i. e., tuberculous myelitis, which offers no chance for restitution.

Tuberculous pachymeningitis is also secondary, as a rule to bone tuberculosis, the extent and its seriousness varying in accordance with the underlying cause; usually the process ends in death, though life may be prolonged and the disease remain stationary. There are but 74 authentic cases of spinal tuberculous pachymeningitis in medical literature (Bandelier and Roepke).

Myelitis.—Evidences of myelitis in a tuberculous subject must always strengthen the diagnosis of *pressure due to bone disease* or secondary deposit in the membranes; in both the symptoms are those of compression and the prognosis is bad.

The prognosis is better in those cases of *tuberculous compression myelitis* due to caries or other bone change in which there has been ossification with latency. In these cases the mischief done cannot be overcome, but

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the process in the cord due to pressure does not advance and there may be slight improvement of the myelitic symptoms. *Extra-medullary tubercle nodules* causing compression myelitis, may, if single, be removed without causing destruction of cord substance and restoration of function may follow. Naturally the prognosis, so far as the life of the patient is concerned, must depend on the extent of the primary disease. It is surprising to note how superficial these nodules are often placed and how easily they may be removed.

Neuritis.—There are occasionally cases of neuritis (peripheral) in tuberculous subjects, which, when a single nerve is involved, frequently yield to treatment, with full restoration of function. When there is *limited compression neuritis,* and the mass, which may be an enlarged gland or tuberculous bone, can be removed, the prognosis is also good. If in such cases there are multiple glandular enlargements at the same time, the advance of the process depends on many factors previously considered; the outlook is not encouraging, though the single neuritis may have been overcome.

Multiple neuritis (*polyneuritis*) of tuberculous origin offers a less favorable prognosis than does single neuritis. It is often a terminal complication with cachexia. In alcoholics it may yield to treatment and disappears; it is then non-tuberculous but alcoholic.

Invasion of the cranial nerves is one of the early evidences of tuberculous meningitis as a rule, and offers a bad prognosis. (See Tuberculous Meningitis.) If there is early involvement of the *pneumogastric* or *phrenic,* death follows promptly. *In children the majority of lesions* (paralyses) *referable to the cranial nerves are secondary to tuberculous basilar deposits;* the correct diagnosis and prognosis need not be long postponed.

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XXI. Rheumatic Fever

(*Acute Polyarthritis, Inflammatory Rheumatism, Rheumatic Fever*)

Acute polyarthritis is an infectious disease in all probability due to the Streptococcus rheumaticus (Poynton and Paine and Rosenow) characterized by constitutional disturbances, inflammatory swelling of several joints in most cases, though the disease may be monarthritic. There is always great tendency to inflammatory changes in the serous structures of the joints involved and in over 50 per cent of all cases there is accompanying endocarditis.

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The disease tends to relapse; following one attack during several years there is great tendency to recurrence.

The disease is most frequent during the winter months (January, February and March) and during this season is likely to be more severe and its duration longer than during the warmer season, though there are many exceptions to this statement.

Bacteriology

The study of the bacteriology of acute rheumatism has not led to positive conclusions until recently, when the observations of Poynton and Paine were confirmed by Rosenow. Poynton and Paine make a strong plea for the acceptance by the profession of their contentions, made during the past few years, that the Diplococcus rheumaticus is the specific microörganism upon which they claim the disease depends.

The bacteriology of acute arthritis has received the attention of many pathologists and clinicians, including Leube, Leyden, F. Meyer, Glaser, Menzer, Sahli, Kraus, Schottmüller, Jochmann, Litten and Lenhartz (See References), without results which to the minds of these observers justified the conclusion that the specific organism has been discovered. We feel safe in concluding, however, that the proofs offered by Poynton and Paine as well as Rosenow justify the conclusion that polyarthritis is an infectious disease and is in all likelihood due to the streptococcus rheumaticus.

Rosenow says: "The name streptococcus rheumaticus may be retained at present, not with the idea that organisms so-called always produce rheumatism, but rather to call attention to the fact that when streptococci produce the symptoms and lesions of rheumatism they have certain special features which streptococci from other sources do not usually have."

Mortality

Rheumatic fever does not offer a serious prognosis. The mortality of all cases may be safely accepted as being between 3.7 per cent and 4.5 per cent. Hoffman found in his analysis of the cases at Johns Hopkins from 1892 to 1911 that the mortality in 70 males was 4.3 per cent without a death among the 15 females reported.

Factors Influencing Prognosis

There are many factors which influence the course of the disease and its severity; the study of its prognosis may be divided into the consideration of:

I. The resistance of the patient.
II. The sex and age of the patient.
III. The character of the onset.

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IV. The nature of chronic preëxisting and acute coincident disease.
V. Complications.
(a) Heart.
(b) Hyperpyrexia.
(c) Brain and Nervous System.
(d) Blood.
(e) Lung and Pleura.
(f) Kidney.
(g) Peritoneum and Appendix.
(h) Skin.
(i) Rheumatic nodules (Meynet).
(j) Septic Conditions.
(k) Purpura.
VI. *Duration.*
VII. Environment and Social Conditions.
VIII. Relapse.
IX. Immunity.

I. Resistance of Patient

As in all acute infections, those reduced in health, the weak, the obese, the alcoholic, and the dissipated, those who have been exposed to the elements without protection, those who work in damp places away from the sunlight and those who seem to be predisposed by heredity, present a lowered resistance, contract the disease after even slight exposure and are more likely than are those without these unfavorable factors to suffer from the severer forms and its complications. Poynton has called attention to the *influence of heredity* in fragile children, "particularly if this be derived from both parents." Such subjects are liable to destructive forms of carditis, to "deadly persistence of the process with increasing anemia, and not infrequently the development of nodules."

There is a greater likelihood of chorea during early life. In children the effect of chorea with severe carditis is always ominous and demands a guarded prognosis. We will again refer to the influence of age in connection with the consideration of the complications.

II. Sex and Age

Sex is not an important factor in prognosis; men contract the disease oftener than women because they are more exposed. The report of Whipham showed among 654 cases, 375 males and 279 females. In our practice the proportion of females to males is 1 to 3; the same proportion is shown in our hospital service. Females in our service have suffered the same complications as men, without material differences in the prognosis.

Between the ages of ten and twenty the proportion of female patients predominates. Kemp found at the Radcliffe Infirmary in Oxford that

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between the tenth and nineteenth year there were among 49 cases 18 males and 31 females, or 47.1 per cent of all of the cases reported. The figures of Church showed 43.5 per cent of 943 cases between the same ages.

Age.—*In children*, the complications, particularly those involving the heart, are more frequent and more serious than in the adult; the disease is not frequent before the sixth year. In young children, *pericarditis* is always a source of great anxiety and *endocarditis* is likely to leave permanent valvular lesions. Langmead reports the "incidence of arthritis in children very high." He examined 2,556 children, of which 133 were rheumatic and in all but 18 the heart was involved. "In 43 per cent of these cases there was some abnormality of the tonsils or pharyngeal mucosa." Whipham reports that of the cases considered, 32 cases were under ten years of age and 80 per cent were between twenty and forty years of age.

III. The Character of the Onset

It is difficult to offer a forecast from the consideration of the method of onset of the disease.

There are *cases which begin without prodromata* but with sudden high fever and multiple arthritis in which the course is short and complications are few; while, often, *cases which begin insidiously* without fiery symptoms, with gradually increasing joint invasions, run a protracted course, including serious complications.

There are cases which begin with high fever, promptly develop *hyperpyrexia* with well-pronounced *cerebral manifestations*, usually the earmarks of *meningitis;* at first there is a full pulse, in which the course is *foudroyant;* death results within the first two to four days. These resemble the *cerebral rheumatism* of the older writers.

Persistently rapid pulse during the early days of the disease with or without high fever must claim the close attention of the attendant, for it may signify *myocarditis* or some other early and serious complication.

Early arhythmia, intermittence or irregularity of the heart, with evidences of myocardial weakness or *dilatation*, influence prognosis unfavorably, both in children and in the adult.

Early profuse sweating, unless accompanied with heart lesions or other depressing complications, is not unfavorable.

Cold extremities, small, rapid pulse with profuse sweating early, is an unfavorable combination.

IV. The Nature of Chronic Preëxisting or Acute Coincident Disease

Preëxisting Diseases.—Preëxisting diseases, particularly those which are depressing, reduce the blood state, cause heart weakness or mental depression, always lower the resistance of the arthritic.

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One of the most important factors in the prognosis of rheumatism is *the condition of the heart previous to the acute attack. Chronic valvular disease* always increases the dangers of arthritis; the nature and extent of the preëxisting lesion is important.

Preëxisting pleurisy, and myocarditis add to the dangers of acute polyarthritis.

When arthritis develops *in a nephritic*, the prognosis must necessarily depend upon the stage of the nephritis, its character and the complications. If there is *chronic uremia*, the added rheumatism will have an unfavorable influence.

With preceding *acute nephritis* following acute infections and added arthritis, the prognosis may continue to be grave and uncertain during varying periods.

Diabetes with acute arthritis superadded, is at times complicated by suddenly arising *acetonemia* and presents a serious prognosis.

With most *chronic diseases* which complicate acute arthritis, the prognosis must depend upon the associated symptoms and added complications. As a rule, the arthritis runs a favorable course and leaves the patient in his previous condition after a reasonable period of convalescence.

The addition of arthritis to *chronic tuberculosis* is considered in connection with the latter subject. (See Tuberculosis.)

Acute Coincident Diseases.—Among the acute coincident diseases with which arthritis is found are *tonsillitis, typhoid fever, typhus, scarlet fever, erysipelas, diphtheria* (*serum sickness*), *mixed infections* and a variety of less frequently arising infections.

Tonsillitis or tonsillar infection of some kind is present in from 70 to 80 per cent of all acute arthritides. Tonsillitis or tonsillar infection, the pathogenic factor of most arthritides, does not influence prognosis unfavorably if the clinician appreciates its significance.

Typhoid and typhus fever with rheumatism are, as a rule, but slightly influenced by the latter disease, for it is likely to be a late complication and in our experience has not often been severe. In children, following closely after typhoid or associated with it, there is greater danger of heart complication and the prognosis is therefore relatively worse.

Arthritis with *scarlet fever* offers a good prognosis so far as life is concerned. In over 90 per cent of cases there is great danger of *endocarditis, nephritis and occasionally pericarditis*, which necessarily influence the course of the disease unfavorably and permanent damage to valves often results, while convalescence may be long postponed and *relapse of the arthritis is not uncommon.*

Erysipelas with arthritis may be either suppurative or non-suppurative. *When suppurative*, the evidences of *sepsis or pyemia* are sufficient to warrant a guarded prognosis. These cases are always serious. *Septic*

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thrombosis with such complications are to be feared. The *non-suppurative arthritides with erysipelas* lead to recovery unless the latter disease is an expression of profound sepsis or both are complicated by serious heart, kidney or brain lesions.

Diphtheria. Serum sickness following the use of antitoxin, with joint swellings and other evidences of arthritis, is of short duration and patients recover.

Acute arthritis with diphtheria is less frequent than with scarlet fever; all of our cases have recovered. There may be sequelæ including damaged endocardium or nephritis. The presence of arthritis does not in any way influence the incidence of *post diphtheritic paralysis.*

Mixed Infections.—Mixed infections are always serious. *Streptococcus or staphylococcus infections are often associated with malignant and septic endocarditis, nephritis, infarcts and justify an unfavorable prognosis.* We will refer fully to malignant endocarditis in another chapter. (See Malignant Endocarditis.) The malignant rheumatic endocarditis of Lenhartz and Litten is also considered with Malignant Endocarditis.

V. Complications

(a) Heart.—Endocarditis.. *In the adult* there is complicating endocarditis in 34.3 per cent (Pribram); *in children* the percentage is between 60 and 80 per cent of polyarthritides, varying during different years and seasons.

Arthritis is the most frequent cause of acute endocarditis and therefore of chronic valvular defects. Bouillard in 1836 made the statement that "with severe and generalized rheumatism, endocarditis is the coincidence, pericarditis or endopericarditis the rule, absence of the latter the exception. . . . With acute rheumatism which is mild, afebrile, partial, endocarditis is not the coincidence, and the coincidence of pericarditis or endopericarditis is the exception."

The prognosis of endocarditis in childhood is less favorable than in the adult. In the adult the majority of endocarditides complicating arthritis make recoveries with but insignificant valvular damage. The larger number of lesions are finally found to change the mitral valve more than any other and the heart soon compensates for the fault.

In both children and adults but few who have relapses escape endocardial infections. Stephen MacKenzie's statistics quoted by Osler show that of 116 cases, 58.1 per cent had endocarditis in their first attack, 63 per cent in the second attack, and 71 per cent in the third attack. In children the acute manifestations of the complication may, during many days, cause great anxiety and make the prognosis uncertain. *When endocarditis and pericarditis are coincident* in the child, or in the adult, the danger is greatly increased, always more in the child.

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Malignant endocarditis at all ages offers the same unfavorable prognosis (see Malignant Endocarditis); it is not frequent with the usual rheumatic infection, but when there is mixed infection, streptococcus or Streptococcus viridans, there is likelihood of endocardial infection. With Streptococcus viridans and pneumococcus endocarditis following or accompanying arthritis, the course is likely to be chronic, particularly with the viridans infection; the outcome is always fatal.

Severe endocarditis in children with chorea and rheumatism is among the most painful of all combinations, and justifies only the most guarded prognosis. In children as in adults many cases of *acute arthritis with dilated hearts* or slight mitral lesion make prompt recoveries and it is not at all unusual to find that the physical signs of endocarditis disappear and subjective symptoms may never recur.

With mild grades of endocarditis in children and chorea, recovery is the rule. If, in these, endocarditis leads to *mitral stenosis,* as it sometimes does in the more chronic cases, the outlook is more serious than without it. If with mitral stenosis in children and adults there are *repeated relapses and fresh endocarditis is grafted on the old,* the prognosis becomes correspondingly worse. It may be positively asserted that with a remnant of endocarditis shown by positive physical signs in adults and in children the prognosis becomes worse with each relapse of arthritis; with these cases, as Poynton has said, "the prognosis, apart from this unknown factor (recurrence), turns mainly upon the condition of the heart." Poynton's conclusions concerning the significance of valvular lesions in children are applicable to the adult as well and they are here quoted:

"(1) Mitral incompetence, if slight and well compensated, gives a favorable outlook.

"(2) Mitral incompetence with a large feeble heart and symptoms of breathlessness and asystole is gloomy; such cases run a very unfavorable course in childhood.

"(3) Slight mitral stenosis is compatible with a long and useful life.

"(4) Progressive and severe mitral stenosis in childhood gives a very grave outlook for the future.

"(5) Aortic and mitral disease combined are very serious when the aortic lesion is well marked; when this is only slight the cases fall into line with those of simple mitral incompetence.

"(6) Primary aortic disease of severity is rare, but the outlook is grave."

It is often surprising to note how desperately ill patients may be with endocarditis complicating polyarthritis, how feeble the pulse and threatening the objective signs and how they may rally to make slow but satisfactory recoveries.

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PERICARDITIS.—Pericarditis complicates from 5 to 6 per cent of adult rheumatism and from 10 to 20 per cent of the cases during childhood. There is, in the majority of severe cases, coincident endocarditis and often characteristic changes in the myocardium, to which we will refer in this chapter.

During early life the prognosis of pericarditis, whether serous or purulent, is less favorable than in the adult. In very young children pericarditis is likely to prove a fatal complication. In children, pericarditis with recurring attacks, in which there is a preëxisting endocardial lesion, proves exceedingly grave. Poynton's experience has been repeatedly confirmed, i. e., that in children, "practically all the fatal first attacks develop pericarditis." *With asystole, adherent pericardium and hypertrophy of the heart*, the prognosis is unfavorable in children; in adults, these conditions are also exceedingly grave.

In both children and adults the majority of serous pericarditides make satisfactory recoveries, though the associated endocarditis may and often does lead to valvular deformity. It is never to be lightly regarded.

In the adult, and in the child, pericarditis is associated with *myocardial change* in many cases, which has a strong influence on prognosis.

Suddenly arising or gradually increasing heart weakness with pericarditis, from whatever cause, clouds the forecast; in most cases it leads to death unless promptly overcome.

It will always be wise to give a guarded prognosis in cases which recover as to the future of the heart, for *slowly forming adhesions* may interfere with the functioning ability of the heart and lead to irreparable *cardiac asthenia.*

MYOCARDITIS.—*Thrombo-myo-endocarditis.*—The myocardium is the most important organ for prognosis in arthritis, as in all acute infections. Myocarditis is present in 15 per cent of all cases.

It may be assumed that *with an unchanged myocardium and the absence of vasomotor paralysis*, the prognosis of polyarthritis is favorable; *with a changed myocardium* the prognosis remains uncertain. Severe rheumatism with endocarditis is usually associated with changes in the myocardium which are characteristic, differing from those found with other infections. Aschoff and Tawara described this peculiar myocarditis of polyarthritis. It consists in a leukocytic infiltration of the myocardium; there are foci of large round cells, mononuclear with basophilic colored protoplasm; there is a unique wreath-form arrangement of the cells. These foci are found in the perivascular connective tissue, they are subendocardial, there is thrombus formation near the surface, producing the thrombo-endocarditis of Aschoff. Poynton and Paine produced this type of thrombo-myo-endocarditis experimentally with the germ which they claim to be the specific organism of polyarthritis (Diplococcus rheumaticus).

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In cases of moderate severity without marked symptoms referable to the myocardium, it is often difficult to tell the depth of the change in the muscle. Subsequent histories prove that unrecognized myocarditis leads to dilatation and faulty function during many months and with added interstitial change may cause permanent damage or death. Most cases of myocardial weakness without valvular lesions in children and in adults eventually lead to recovery. Many systolic murmurs heard during acute polyarthritis are due to myocardial change and are not of endocardial origin. Ventricular dilatation due to myocardial weakness may cause these and they usually disappear as the relative insufficiency is relieved. The strength of the myocardium or the "heart's working capacity" is best tested by learning, as Kemp has claimed, the "amount of physical work which each individual can do in earning his or her living." This naturally requires a full consideration of the individual case after the period of convalescence.

Sudden Death.—Sudden death is not frequent. As a rule it is due to myocarditis, thrombosis or embolism. With *hyperpyrexia* death may be sudden. We have seen such patients die within a few minutes after convulsions.

Blood Pressure.—At the height of the attack blood pressure is usually low; in the average adult and moderately severe polyarthritis it averages 100 mm. Hg. *Hypotensive conditions* which increase or persist influence prognosis unfavorably.

With marked myocarditis rheumatica (Aschoff type) the prognostic conclusions will be materially strengthened by the intensive study of blood pressure. High blood pressure early, with tense pulse and previous nephritis, is unfavorable. In patients whose previous history is vague, with persisting high blood pressure during the height of the disease, the preëxistence of *chronic nephritis* may be strongly suspected and the prognosis may be accordingly framed.

Bradycardia.—Bradycardia during convalescence is not serious. It often follows cases of long duration in which digitalis has been given. It may follow under other conditions. In old patients with arteriosclerosis it may indicate heart-block (Adams-Stokes phenomenon) and it is serious. *With meningitis* bradycardia may be present early, but does not continue long and is soon followed by a small rapid and compressible pulse.

Tachycardia.—Persistent tachycardia during the acute period is a grave symptom, particularly if there is progressive lowering of blood pressure with other evidences of myocardial weakness.

(b) Hyperpyrexia.—Rheumatism is one of the three conditions which may be associated with the highest temperature found in the practice of clinical medicine. (The other two are sunstroke and meningitis.) The modern treatment of arthritis has unquestionably reduced the incidence

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of hyperpyrexia. Hyperpyrexia with rheumatism is more frequent in hospital than in private practice.

Hyperpyrexia is always life threatening; there are usually symptoms referable to the meninges, kidney, and to the heart. Wild and active delirium is followed by coma; these symptoms may follow each other in rapid succession. The patient is cyanosed, conjunctiva is congested, Kernig symptom is present, there may be convulsions (particularly in children), there is albuminuria, concentrated and acid urine, materially reduced in quantity and evidences of rapidly failing heart strength. In some cases there are paralyses with spasticity.

The *duration* of cases with marked hyperpyrexia is short. Death may follow in from twelve to forty-eight hours. Many of these cases are the prototypes of Trousseau's "*cerebral rheumatism.*"

With hyperpyrexia, *the prognosis is almost always fatal.* We have never seen recoveries, when, with the symptoms mentioned, the temperature has mounted above 106°F. In rare cases the temperature may reach as high as 108°-110° before death.

(c) Brain and Nervous System.—Meningitis (see Hyperpyrexia, preceding paragraphs) is usually a fatal complication of rheumatism. There are cases of *transitory meningismus* in children and in adults which recover without the development of active or progressive meningitis.

Delirium and other mental symptoms are not uncommon during the acute period; these are not of serious import in most cases. But few severe or widespread arthritides are exempt from psychic disturbances. They are often marked in young subjects, in alcoholics and in the plethoric; but are by no means limited to these. *Acute psychoses* are occasionally present with *hallucinations;* at times *active mania* and *manic-depressive states, also stupor.* These conditions are rarely lasting, they are of toxic origin and yield in the course of a few weeks to several months.

Neuritis may be either an early or a late complication. There may be *multiple neuritis* or a single nerve trunk may be involved. Most peripheral neuritides are associated with more or less *muscular atrophy.* The *single neuritides* may include either the *sciatic,* the *motor oculi,* the *trifacial* or other nerves.

The prognosis of all forms of neuritis with arthritis is good.

(d) The Blood.—Uncomplicated cases of polyarthritis with fever and joint swelling show an average *leukocytosis* of 15,000; higher counts are rare. Serious infections with complications such as pleurisy, pericarditis, pneumonia, etc., present much higher leukocytic counts.

Improvement, fall of temperature and reducing swelling of the joints, is followed by a lowered leukocytic count. Fresh infection may be suspected when there is a sudden leukocytic increase. Naegeli showed that there is a decided *neutrophilic* increase, occasionally *mononuclear* also.

At the height of the acute symptoms there is a decided decrease of

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lymphocytes and eosinophils; an increase of these is found with improvement of constitutional and local symptoms and argues in favor of an early convalescence.

Anemia is characteristic of acute arthritis, there is a prompt destruction of erythrocytes in severe cases, and the blood elements including the red corpuscles and hemoglobin reform very slowly during convalescence. *Persistent anemia* is always a serious indication. *Fibrin and blood plates* are always increased.

Cases beginning with typhoid symptoms, in which there is *slight enlargement of the spleen* (Naegeli), may prove puzzling for diagnosis and prognosis. In these, the leukocytosis and increase of fibrin preclude the possibility of typhoid. Joint symptoms develop after from thirty-six to sixty hours in most cases.

(e) Lung and Pleura.—PNEUMONIA.—*Croupous or bronchopneumonia* may complicate rheumatism. Pneumonia is an occasional terminal infection *in alcoholics,* in the aged or in children. *Croupous pneumonia* is not often the cause of death. When *pneumococcemia* or other types of pneumonia are complications, they are secondary. (See Pneumonia). Hypostatic bronchopneumonia may complicate the more serious and persistent cases. (See Bronchopneumonia).

PLEURISY.—Pleurisy may be due to extension from the pericardium; when associated with endocarditis and pericarditis, in the presence of large serous effusion it adds to the discomforts of the patient and to the dangers. *Recovery* is possible and follows in a large proportion of cases. It has been our experience that the exudate is promptly absorbed, also that the symptoms yield to one or two aspirations.

The association of pleuritis and pericarditis (polyserositis) was found by Mosler in 15 of 142 cases of arthritis; in these the prognosis cannot be given early. The cases demand long periods of observation that the resulting adhesions and heart damage may be considered.

EMPYEMA.—Empyema does not often complicate rheumatism; when it does it is secondary. It yields to radical treatment unless the underlying sepsis or pyemia is overpowering.

BRONCHITIS.—Bronchitis associated with rheumatism, unless secondary to serious heart lesions, is usually insignificant.

(f) Kidney.—ALBUMINURIA with rheumatism does not necessarily indicate the presence of nephritis and though frequent, particularly during the febrile period, it is not *per se* of serious import.

CONCENTRATED ACID URINE is the rule and does not materially influence the course of the disease. It offers indications for treatment, which when recognized, can in most cases be controlled.

NEPHRITIS is a rare complication. With *mixed infection,* cases that prove to be septic, or with infarct due to malignant endocarditis, renal changes are ominous.

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(g) Peritonitis and Appendicitis.—In a large experience we have met but one case of RHEUMATIC PERITONITIS; it ended fatally. Jochmann has never seen a case.

APPENDICITIS is in some cases held to be of rheumatic origin. There are cases which remain unexplained; some are associated with or follow tonsillitis; it may be that these are dependent upon the same infection. However, the question is still *sub judice;* Poynton and Paine have caused it experimentally with an organism which they isolated from cases of rheumatism.

(h) The Skin.—SUDAMINOUS ERUPTIONS are the rule and are unimportant prognostically.

ERYTHEMATOUS ERUPTIONS, *intertrigo* and occasional herpes, are without prognostic significance.

ERYTHEMA NODOSUM.—Erythema nodosum is unquestionably of infectious origin and presents many of the earmarks of rheumatism and should in the present state of our knowledge be classified with it. Children suffer oftener than adults. Only rarely are there serious complications referable to vital organs (heart, etc.). The prognosis is uniformly good. The duration varies, the disease may run an acute course in seven to ten days, may show tendency to relapse, may become subacute and in rare cases, usually in the adult, becomes chronic.

(i) Rheumatic Nodules (Meynet).—These nodules first described by Meynet are about the size of a pea, rarely larger; they are located on the fingers, hands, wrists and in the neighborhood of the elbows. They rarely form during the height of the disease, usually follow the febrile period. Osler says they are common in children with mitral lesions. All authors have found the nodules oftener in children than in adults.

Kemp holds that "the presence of rheumatic subcutaneous nodules has a definite bearing on prognosis, and when present, especially in children, are always accompanied by gross damage to the heart." They are more frequent in children than in adults. They probably hold infecting agents and are responsible for fresh attacks. Rheumatic nodules do not influence prognosis in adults materially.

(j) Septic Conditions.—The septic condition is due to mixed infection, is always serious when complicating rheumatism. It may be either early or late and is likely to be associated with septic endocarditis, septic thrombo-myocarditis and offers an unfavorable prognosis (See Sepsis and Malignant Endocarditis).

In occasional cases symptoms of septic fever precede polyarthritis (non-suppurative) during several days before there are positive evidences of joint disease. Many of these recover.

Sepsis is in rare cases associated with multiple suppurative arthritis. In some of these, the septic condition precedes the joint symptoms during several days. Thorough search usually reveals the primary focus. Our

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experience with these cases has been unfavorable; they often present the clinical picture of malignant septicemia.

(k) Purpura.—Whether purpura rheumatica should be included in the consideration of polyarthritis remains undecided. In this work it will be separately considered (See Purpura).

Purpuric and hemorrhagic conditions complicating arthritis are always suggestive of malignant infection and demand a guarded prognosis. When purpuric conditions are due to *hemophilia* or are attributable to the usual causes of non-malignant purpura (purpura simplex, rheumatica, and hemorrhagica) the prognosis of arthritis is not unfavorably influenced by the complication; on the other hand, septic conditions, with limited or extensive petechiæ, with or without endocarditis, are always serious. These conditions are embolic.

Blebs or vesicles which contain blood often show a tendency to *necrobiosis* of the underlying cutis, are also of *embolic origin*, and are evidence of *malignant infection*.

VI. Duration

It is never safe to make a prophecy which will commit the clinician to a time limit of polyarthritis. It is absolutely impossible in any case to give any reliable information on the subject, for apparently mild cases at the beginning finally prove to be rebellious to treatment and those in which the initial symptoms argue in favor of a long period of arthritis often run a short course.

Number of Joints Inflamed.—The early and persistent inflammation of a single joint (*monarthritis*) in the majority of cases argues in favor of a slow process and occasionally leads to *subacute disease* or *chronicity*. In rheumatism the prognosis as to length of time the disease lasts seems, as the result of the observation of many clinicians, in many series of cases, to be less favorable when the disease is monarticular and stationary, than with the invasion of several joints or the leaping of the disease from joint to joint. If with *polyarthritis* the features of the disease change, and one joint is selected with tendency to thickening and swelling, a long period may be expected during which the local and some constitutional symptoms will continue troublesome. *Migratory lesions* of the joints often yield within a reasonable period.

Recurring rheumatism is usually either subacute or may approach chronicity. It is not at all unusual to find the second or the third attack associated with endocarditis and multiple joint invasion continuing during four to eight months. The average duration of the benign case is from three to six weeks.

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VII. Environment and Social Conditions

In considering the factors which influence the course of the disease we referred to sunlight, dampness and other baneful conditions which lower the resistance of the patient; these are also included in the study of the environmental and social factors which influence prognosis. Unhealthy homes, faulty ventilation, insufficient and faulty food, humidity, exposure, dissipation, excesses of all kinds prepare the culture media within the body which are needed for the proliferation of the micro-organism which is the cause of the disease.

It is not at all unusual to find patients who have suffered repeated attacks of arthritis relieved permanently by a change of residence or climate; in other cases, change of occupation and methods of living prove to have a wholesome influence.

VIII. Relapse

Relapses are frequent, and exert an enormous influence on the subsequent history of these patients because endocardial complications are aggravated and valvular deformities are thereby increased. Relapse often leads to chronic changes in the joints with deformities and *muscular atrophies*. Muscular atrophies increase with each attack of rheumatism, particularly with those forms in which the symptoms continue subacute during long periods and remain limited to the same joints.

IX. Immunity

Arthritic infection is not followed by immunity. In many a predisposition is developed which invites repeated attacks. It not infrequently happens that the predisposition continues during four to six years following the initial attack, after which there may never be a return of the disease. These facts thoroughly appreciated by life insurance companies have led to the postponement or rejection of applicants during a number of years after acute attacks of arthritis.

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XXII. Tonsillitis

The Influence of the Tonsil on Prophylaxis and Prognosis

The tonsil serves as the *port of entry* of pathogenic organisms and has an enormous influence in spreading infection to distant organs through the chain of lymphatics with which it is intimately connected and through the blood-stream. The normal tonsil harbors disease-producing micro-organisms at all times; the diseased tonsil is a greater menace, for in its crypts conditions are offered which invite local proliferation and consecutive constitutional infection.

All changed, enlarged and adherent tonsils powerfully influence the prognosis of many pathologic conditions. I considered the influence of the tonsils in connection with the study of tuberculosis. (See Tuberculosis.) Recent investigations by Mitchell dealing with the infection of children with bovine tuberculosis accent their importance and prove the enormous influence of the faucial tonsils in tuberculosis of the upper cervical glands; they also prove that *in a large proportion of cases* a well-marked tuberculosis of the deep glands "is secondary to a small tuberculous focus in the tonsil." In children, Mitchell reports the "high percentage of faucial tonsils in which the bovine virus was present," and claims it "is further striking proof of the frequency of tuberculous cows' milk as a source of infection." Wood in 1,671 cases showed that in 88 (or 5.2 per cent) the tonsils were tuberculous. Lartigan contends that Wood's figures are less reliable than his own in which he did not rely upon histologic studies alone, but added the results of inoculation tests and found that 12 of his 75 cases gave positive results to animal inoculation and therefore placed the percentage of tubercular involvement of the pharyngeal tonsil at 16.

Tonsils in which there are no apparent changes have been proved experimentally and clinically to hold the organisms of cerebrospinal meningitis, pneumonia, rheumatism, streptococcus endocarditis, poliomyelitis and many other grave diseases, and have served as the port of entry of these disease-producing agents.

Further it may be contended with considerable certainty that *many chronic disases, the causes of which have not been understood in the past, are being favorably influenced by the enucleation of both large and small*

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tonsils. Among these diseases are the various forms of so-called *chronic rheumatism and rheumatoid arthritis.*

There are *acute infections of the tonsils* in which these organs are involved. Among these are *diphtheria and suppurative peritonsillitis.* To such tonsils, after convalescence has commenced, serious constitutional disturbances which threaten life may be traced; they continue to hold in their crypts and tissues colonies of the original pathogenic microörganism which they throw into the blood-stream from time to time. *Pyemia, sepsis, nephritis* and other infections have followed from such source.

Diphtheritic paralyses, in which there are acute exacerbations with evidences of *sensory neuritis,* have been favorably influenced by the enucleation of tonsils, in which, weeks after the acute process had run its course, diphtheria bacilli were found.

In a number of cases of *Hodgkin's disease* there has been a clear history of persistent enlargement of cervical glands following tonsillar infections. In some of these, the glands remained stationary during a number of months before showing the progressive enlargement and extension of the fatal disease.

The prophylaxis and prognosis of many constitutional diseases as well as many conditions, the cause of which we have been unable to understand, will be favorably influenced by the thorough appreciation of the importance of the faucial tonsil as a reservoir from which many and serious infections may proceed, and the further fact that the defensive function of the organ is readily overcome.

Acute Follicular Tonsillitis

Angina, Amygdalitis, Streptococcus Tonsillitis

Tonsillitis is an acute infection of the tonsil leading to inflammation, membranous deposit, constitutional disturbances, occurring usually during early life, with complications either early or late which may lead to grave organic changes in one or more organs. It may be *sporadic* or *epidemic.* Most acute tonsillitides are of *streptococcus origin.* The majority of these run a favorable course and lead to convalescence with considerable weakness, and at times long periods of ill-defined symptoms with a general condition below par.

Sporadic Cases.—There are ACUTE SPORADIC CASES in which, for several days, there are free and outspoken *constitutional manifestations,* including, with the tonsillar lesions, high temperature, rapid pulse, mitral systolic murmur due to muscular insufficiency and albuminuria; often there are evidences of nephritis. These cases under treatment and rest offer a good prognosis; rarely does death follow except in those reduced by previous disease, burdened by depressing and undermining diatheses or some one of the early complications to be mentioned later.

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The subsequent history proves the importance of the infection as a cause of chronic and permanent disease in neglected and malignant streptococcus infections. In all cases the extent of the glandular invasion (enlarged cervical glands) is an index of the depth of the infection.

There are all grades of severity in the sporadic cases.

STREPTOCOCCUS TONSILLITIS may accompany and materially influence the course of other infections; among these are *influenza, measles, scarlet fever, infantile paralysis, cerebrospinal meningitis, and in young children bronchopneumonia occasionally.* In rare cases it may precede these infections.

Sporadic cases may infect entire households or wards of hospitals and it sometimes happens that an outbreak of streptococcus tonsillitis in a surgical ward leads to erysipelas among the operated cases.

MILD SPORADIC CASES run their course in from three to six days. Those with marked constitutional disturbances average between six and nine days.

Convalescence is usually slow, sequelæ are numerous and often serious. These will be considered with the epidemic type of the disease.

Endemic and Epidemic Streptococcus Tonsillitis.—The most frequent source of endemic or epidemic tonsillitis is infected milk. The infection is almost always due to organisms belonging to the streptococcus group. Miller, who investigated the Chicago epidemic, found that "an epidemic of mastitis existed in cows and sore throat in farmers" in the territory which supplied the contaminated milk, and emphasizes the fact that "streptococci which cause mastitis in cows may be pathogenic for animals and virulent to man."

Epidemic streptococcus tonsillitis which prevailed in Cortland and the adjacent counties of Central New York during 1912 was virulent and was the cause of many deaths. The old and feeble, also very young children offered lowered resistance. The complications of the Cortland epidemic were numerous and included nephritis, endocarditis, pneumonia, metastatic parotitis (see Metastatic Parotitis) and a variety of conditions which lead to tardy convalescence.

Capps and Miller made an exhaustive report of the Chicago epidemic due to the contaminated milk supply above mentioned; 10,000 cases were included.

Epidemic cases are always much prostrated by the infection and show marked leukocytosis.

Second attacks within a few days are frequent and lead to slow convalescence.

Capps and Miller report *peritonsillar abscesses* in occasional cases which, when promptly opened, lead to prompt recovery.

Complications.—*The unfavorable cases are those in which there is bacteremia, which leads to numerous complications. Otitis media* compli-

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cated 6 of 173 typical cases observed by Capps and Miller. *Arthritis* is a frequent complication of epidemic tonsillitis; it is present in 10 per cent of the cases and occasionally leads to suppuration of the joints. *Erysipelas* complicated two cases seen by us during the epidemic in Cortland and adjoining counties. In one, the complication was migratory, covered the entire body in its acute exacerbations; the patient, a man aged about thirty, finally developed *streptococcus meningitis* and died. The other case was a woman who recovered. She was over seventy, developed secondary pneumonia, suppurative metastatic parotitis and erysipelas, after initial streptococcus tonsillitis.

Nineteen of the 173 cases reported by Capps and Miller died. Nine of these died of peritonitis, four of pneumonia and three of septicemia. An investigation made at the time of the Cortland epidemic by Dr. Charles E. North of New York City, who, with two assistants, coöperated with the Public Health Committee of the Cortland County Medical Society, resulted in the finding of two cows in one dairy that were affected with garget. This dairy furnished about 7 per cent of the total milk supply and tabulation showed that this dairy furnished milk to families in which about 72 per cent of the whole number of cases occurred. Eleven throat cultures were examined and all of them revealed the presence of a certain species of streptococcus of the same type found in the discharge from the udders of the two affected cows. Of 669 cases 13 died, cause of death as follows:

Age.	*Cause of Death.*
50	Edema of Larynx.
51	Heart Failure.
69	Lobar Pneumonia.
39	Peritonitis.
66	Peritonitis.
60	Peritonitis.
62	Peritonitis.
70	Erysipelas.
80	Erysipelas.
82	Pneumonia.
72	Heart Disease.
78	Erysipelas.
Unknown	Peritonitis.

In addition, there were reported seven other cases of erysipelas; nearly all cases had enlarged cervical glands, many of them forming abscesses; and a very large number of protracted cases of rheumatism. Also cases of pleurisy and pericarditis.

Epidemic cases occasionally run a prolonged course—three to seven weeks, after which the convalescence is slow and the patient continues weak during a long time. Mild cases recover in from two to three days.

Heart Complications.—The cardiac complications which follow all

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forms of tonsillitis may be either due to *streptococcus endocarditis* and *myocarditis, to relative insufficiency of the myocardium, to functional disturbances depending on the reduced state of the patient* or to *distant complications, such as nephritis, arthritis,* et cetera. All of these offer a favorable prognosis except those forms of malignant endocarditis of streptococcus origin. Permanent damage often follows in the non-malignant cases and the patient recovers with an irritable heart and valvular lesions. In these cases, either with subsequent tonsillitis or without, there are *acute endocardial exacerbations* in which there may be complications which are serious, *including nephritis and possible cardiac insufficiency and increasing anemia.* Many of these patients fall into extremely dangerous conditions including general dropsy, from which they may with proper care and treatment recover, i. e., return to their former state with an added endocardial scar.

Pericarditis if *purulent* complicating or following tonsillar infection is always serious.

Not all *murmurs* following streptococcus tonsillitis are due to endocarditis. The majority of mitral systolic murmurs are due to relative muscular insufficiency and disappear as the patient regains strength.

Chorea is frequently associated with an initial tonsillar infection; there is with these cases often acute endocarditis. The prognosis is good; in obese children endocarditis may be severe and occasionally, without relief of the choreic symptoms, the child dies. *Malignant endocarditis may prove to be a sequel.*

Functional disturbances causing arhythmia and annoying intermissions and irregularities also yield after long periods of rest.

Bradycardia is an occasional sequel or an accompaniment of the acute stage, without unfavorably influencing the prognosis.

KIDNEY.—*Nephritis,* which follows within seven to twenty-one days after acute tonsillitis, is often rebellious and occasionally leads to *dropsies* and to *fatal uremia.*

Early nephritis and albuminuria usually yields during the slow convalescence.

ARTHRITIS (*Rheumatism*).—*Arthritis* is a frequent complication of tonsillitis and shows the characteristics of *polyarthritis* in most cases, is often complicated with endocarditis, is subject to relapse and usually leads to full recovery without permanent damage to the joints invaded. (See Polyarthritis.)

PARALYSIS.—We have never chanced to find a single case of paralysis in which the bacteriologic diagnosis of streptococcus tonsillitis was positive. Such cases are recorded, but must be exceedingly rare.

SEPTICEMIA *without evidences of local disturbance or with endocarditis* is the most serious sequel of tonsillitis. It offers only the most unfavorable forecast.

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Among the OTHER COMPLICATIONS of streptococcus tonsillitis are *osteomyelitis, appendicitis, empyema, liver abscess, perinephric abscess, meningitis, and empyema.* (See separate chapters for further prognostic data.)

PNEUMONIA.—The prognosis of *streptococcus pneumonia* following tonsillitis depends on the factors fully considered in connection with the pneumonias. (See Pneumococcemia.)

Generally speaking it may be concluded that the *migratory types* of the disease offer a grave prognosis, the acute cases justify the figures and conclusions to which reference has been made elsewhere. (See Migratory Pneumonia.)

MORTALITY.—Our average *mortality* of all forms of streptococcus tonsillitis in private practice does not reach 2 per cent. Hospital statistics include neglected cases and show a higher mortality.

Phlegmonous Tonsillitis. (*Septic*)

In occasional infections there are marked constitutional symptoms, *nephritis, large albumin loss and destructive gangrenous changes in the tonsils, foul smelling with symptoms of deep sepsis at once, including delirium and final coma which lead to death in from three to seven days.* These cases are rare, they occur in adults as a rule, and before death show decided purpuric tendencies; *they are not to be confounded with suppurative tonsillitis.*

Acute Suppurative Peritonsillitis

Quinsy, Peritonsillitis

Most forms of *quinsy* invade, besides the tonsil, the *peritonsillar tissue;* they may be either *primary or secondary.*

When secondary the suppuration may be a complication of general infection (*pyemia, septicemia, scarlet fever, typhoid, erysipelas, et cetera*) *or it may be associated with nephritis, diabetes or other constitutional diseases. Syphilitic* and *carcinomatous* ulcers at times lead to tonsillar suppuration.

Most primary suppurative peritonsillitides offer a good prognosis if rationally treated.

Edema of the glottis and larynx is at times a sudden complication with both primary and secondary tonsillar suppuration and unless promptly relieved by surgical means ends fatally. *Edema of the uvula* complicates all cases of suppurative peritonsillitis.

The *prognosis of the acute secondary suppuration of the tonsil per se* is not bad; occasionally it suddenly leads to edema particularly in cases of chronic and acute nephritis and threatens life. *The nature of the*

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primary disease naturally influences the prognosis of the associated suppuration, but as a rule the patient recovers from it.

Some subjects develop primary suppuration of the tonsil and peritonsillar tissue repeatedly at short intervals; in almost all, the prognosis is good and *recurrence is prevented by the excision of the tonsils.*

Ulceration of large arteries with consecutive bleeding (internal carotid artery) is exceedingly rare.

Convalescence is often very slow and patients are subject to many of the complications of acute non-suppurative tonsillitis. (See Acute Tonsillitis.)

(e) *Vincent's Angina*

Vincent's angina is due to a fusiform bacillus which may also cause noma (see Cancrum Oris), laryngitis, pneumonia, mastoid inflammation and bronchopneumonia. The bacillus was found by Tunnicliffe to be the pathogenic germ in a case of pyemia. The germ is usually found in connection with other disease-producing organisms (aerobic). Halsted says that "like the other organisms with which it is associated, it occurs in healthy mouths, but more particularly in mouths and throats in which there is some unhealthy condition, such as diseased tonsils, decayed teeth and inflamed gums" . . . "it rarely produces disease when the tonsils, teeth and mucous membranes are in a normal condition."

Vincent's angina may accompany any of the tonsillar infections of diphtheria, scarlet fever, syphilis, streptococcus or other inflammations associated with the formation of false membranes.

Rolleston in 18,187 cases in which diphtheria was suspected admitted to the London Metropolitan Hospital Board that he found during 1905-1907, 3,047 non-diphtheritic cases; of this number 95 were due to the fusiform bacillus, or Vincent's angina.

The disease presents in an ulcerative or destructive form, or remains membranous. Two cases reported by Halsted proved to be fatal. Pearce in his cases found great prostration with feeble and rapid pulse, marked involvement of the nervous system, the hippocratic facies and death from toxemia.

Purpuric symptoms argue in favor of malignancy of infection, as does also necrosis of included tissue. The clinical picture of the malignant cases is much like the fatal cases of cancrum oris.

The prognosis is worse in patients who are reduced and previously infected. The limitation of the disease to the tonsils without marked constitutional symptoms offers a good prognosis. Invasion of the larynx adds an enormous element of danger, particularly during early life.

Non-diphtheritic membranous croup and tonsillitis should always create a suspicion of Vincent's angina. The diagnosis can be cleared only by bacteriologic tests.

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Ulcerative stomatitis may be caused by the fusiform bacillus without involvement of the tonsils. (See Ulcerative Tonsillitis) (Aschoff.)

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Chronic Tonsillitis

(*Chronic Naso-pharyngeal Obstruction, Mouth Breathing, Aprosexia, Adenoids of the Pharynx*)

Chronic tonsillitis may result from preceding acute tonsillar infection and may include persistent enlargement of the neighboring lymphatic glands or it may be a part of a chronic hypertrophy of all the adenoid tissues of the pharynx in which the vault of the pharynx is occupied by succulent adenoid structures which cause mouth breathing and many secondary changes.

The influence of adenoids and chronic enlargement of the tonsils on the growing child is paramount. Development, both mental and physical, is impeded by the handicap which results. Insufficient oxygenation is one of the results of the obstructed breathing. The advance of rhinology has been of great value in calling the attention of the profession to the far-reaching effects of chronic tonsillitis, adenoids and associated lymphatism.

The *facies* of the children suffering from adenoids are characteristic. The direct results of faulty breathing due to the disease are, besides those mentioned, developmental anomalies of the thorax, chicken breast, barrel chest, and funnel breast. *Deafness or faulty hearing is frequent. Convulsive tics are occasional.* These children are hypersensitive, contract the acute infections which spread from the tonsils oftener than do normal children, their breaths are offensive, the crypts of the tonsils hold foul-smelling cheesy masses and when they develop scarlatina the throat symptoms are always severe. The removal of the tonsils and the adenoids promptly changes the picture and from a stupid, mouth-breathing, sickly and apathetic youngster, there is a complete metamorphosis to a normal child in almost all cases. Captain Catlin in his pamphlet published in 1861 probably overestimated the importance of adenoids and enlarged tonsils when he contended that to these anomalies all of the ills of mankind are attributable, but there is much of value and truth in his aphorism "Shut your mouth and save your life."

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Hoffman shows the mortality from all diseases of the tonsils to be 1.8 per cent in males and 1.1 per cent in females including 225 cases.

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XXIII. Metastatic Parotitis

(*Secondary Parotitis, Infectious Parotitis, Parotitis metastatica*)

Inflammation of the parotid not due to epidemic mumps may be considered to be *secondary* to existing infection, is usually *one-sided* and an expression of grave constitutional invasion and malignancy of the primary disease.

The *infections* to which parotitis has been added include all forms of *pyemia, typhoid fever, scarlet fever, pneumonia, dysentery, cholera asiatica, malignant endocarditis, streptococcus infections, sinus thrombosis, cerebrospinal meningitis, small pox, angiocholitis, yellow fever, all nasopharyngeal infections, syphilitic ulcerations of the mouth, peptic ulcers, measles, tuberculosis* and in rare cases *mild infections* and *mumps* lead to *chronic enlargement of the gland.*

Many of these *metastases are due to direct infection through the mouth* and some of these might be prevented by more thorough cleansing of the upper air passages and the nasopharynx, more particularly, than is usually practiced.

The *glandular ducts* and *gland substances* themselves may serve to infect and finally a large number of *secondary parotitides* may be traced to infection through the *blood stream.*

During a recent large epidemic at Cortland, New York, which was traced to *milk infection*, of *streptococcus origin*, I saw a case with Dr. Higgins of *streptococcus tonsillitis* in a woman over 70 years of age who developed *streptococcus pneumonia*, then *streptococcus parotitis*, with small pockets of degeneration and suppuration, who finally made a full recovery. This history with its fortunate outcome is rarely repeated. With most serious infections the development of *secondary parotitis* may be viewed with concern. It is an *evidence of the gravity of the original infection and adds an element of danger at the same time.* In some cases *suppuration advances to the cellular tissue* of the neck (*Angina of Lud-*

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wig) and to the ear and skull, when sub-acute and chronic infection may follow with *facial paralysis, caries or meningitis. Tuberculosis* invading the parotid may cause *caseation.*

Metastases to the parotid occur with equal frequency in children and adults. *Early metastases* to the parotid are more serious than the late infection of the gland. The invasion of the parotid during *acute gouty arthritis* is a painful and weakening complication which, as a rule, yields to treatment in from two to three weeks without suppuration.

C. Diseases due to Non-Bacterial Fungus Infection

1. Actinomycosis

(*Strahlenpilzkrankheit*)

Actinomycosis is caused by the *Actinomyces bovis* (Ballinger, 1877), also known as the "*ray fungus,*" which is a Gram-positive *streptothrix.*

The disease is found in animals—horses, pigs and other cattle—most frequently involving the jaw, mouth and tongue, and is in all probability caused by the eating of ordinary grain or barley holding the actinomyces. Man is more frequently infected than woman (3-1).

The disease leads to a condition of *subacute or chronic pyemia* due to the infiltration and suppuration of the infected tissues, around which there is promptly connective tissue proliferation. In man as in cattle the *jaw* and *tongue* are the usual foci of the disease, though other parts of the body may be infected. The actinomycetes as they enter the tissues cause hyperemia, infiltration, chronic suppuration and consecutive constitutional disturbances. The diagnosis can be made positive by the presence of the ray-fungus in the pus.

The characteristic swellings of the disease may follow in any part of the body to which the streptothrix is carried and the fungus may migrate to surrounding tissues and organs or in severe cases blood vessels may be invaded, more particularly veins, which opens the avenues for the entrance of actinomycetes into the blood stream and their dissemination to distant organs (lung, liver, brain, etc.).

Forms of Actinomycosis

The disease may invade:

1. The alimentary tract
2. The respiratory tract
3. The skin
4. The brain or other internal organs.

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1. Alimentary Actinomycosis.—The course of alimentary actinomycosis, the most frequent form of the disease, is characteristic. The fungus finds a point of entrance in the mucosa surrounding carious teeth, through the mucosa of the floor of the mouth or through the tonsils. The changes already mentioned promptly follow; the local swelling depends upon the direction of growth and the extension of the fungus and the amount of infiltration and suppuration. As a rule there is more or less *periostitis of the jaw* and there are *fistulous tracts* which discharge a thin yellow pus, in which the yellow ray-fungi are promptly detected.

The *tongue* is less likely to show suppuration than the surrounding tissues, but the separate nodules are readily palpated.

The *posterior pharyngeal wall* may be invaded when the disease may extend downward attacking *the esophagus* which it may perforate. As the process progresses the *stomach* and *intestinal mucosa* may be infiltrated.

Perforative peritonitis due to *intestinal perforation* may follow.

Appendicitis develops in occasional cases. Intestinal actinomycosis may lead to *fistulous openings through* the *abdominal wall, to abdominal swellings and adhesions* of *intestines* or to *intestinal stenosis.* The *posterior mediastinum* may be attacked through migration of the actinomyces and the pleura and the lungs invaded through this avenue.

2. Actinomycosis of the Respiratory Tract.—Actinomycosis of the respiratory tract is rare, save as it is secondary to alimentary invasion or follows the aspiration of infected foreign bodies. The fungus causes an obstinate *fetid bronchitis* or as a rule the dependent part of one lung is slowly infiltrated (*chronic pneumonia*) causing constitutional symptoms, including fever, rapid heart action, increasing emaciation, and the expectoration of purulent sputum, with fungi and acid crystals.

In chronic cases there is advance to the *pleura* and to the chest wall, with chronicity and consecutive *deformity.*

In *pulmonary actinomycosis* the *pericardium* may also be the seat of deposit.

3. The Skin.—The skin, through an abrasion or wound may be invaded by the fungus and multiple lesions result with the symptoms of chronic pyemia accompanying the suppuration.

4. The Brain and Other Internal Organs.—The *brain* and *liver* invasions are found in those cases in which the actinomycetes have *invaded the walls of a blood vessel* and have been carried to these organs through the *blood stream.*

In the *brain* the *symptoms of tumor* are prominent and death is the result, the duration varying in accordance with the location of the deposit.

The *liver,* when involved, presents the symptoms of abscess of that organ and offers an unfavorable prognosis unless the abscess is superficial and operable.

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Prognosis of Actinomycosis

The *prognosis* of all forms of actinomycosis must depend on the location of the disease, the ability to remove the focus early by radical surgical treatment. *When the disease is disseminated the chances of recovery by medical treatment are small.*

Spontaneous recoveries have been reported, but are rare and can only be imagined to have followed limited swelling. The *chronic pyemia* of unrelieved cases with its long periods of *remittent fever* leads to exhaustion, emaciation, and after months of suppuration, with increasing anemia and edema, albuminuria with other positive evidences of far-reaching amyloid degeneration of the internal organs develop and death results.

It may be positively concluded that the *skin infections* offer the most favorable prognosis. When the neck and face are the seat of the disease, Poncet and Thevenot found that death followed in one case in 16; with lung and abdominal (visceral) actinomycosis 25 per cent died.

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D. Diseases due to Metazoan Parasites

(*Internal Parasites*)

Of the animal parasites which infect the body (non-microscopic), (1) the tapeworms or *cestodes,* and the (2) round worms, or *nematodes,* are the most important.

1. The principal varieties of the Cestodes are:

(a) *Tenia solium.*
(b) *Tenia saginata or mediocanellata.*
(c) *Bothriocephalus latus.*
(d) *Tenia echinococcus (or hydatids).*

2. The Nematodes are:

(a) *Ascaris lumbricoides.*
(b) *Oxyuris vermicularis.*
(c) *Ankylostomum duodenale or hookworm.*
(d) *Tricocephalus dispar.*
(e) *Trichina spiralis.*
(f) *Filaria sanguinis hominis.*

3. The *Bilharzia hematobia* belongs to the Trematodes and also demands consideration.

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1. Cestodes

(*a*) *Tenia solium*

(*Armed Tapeworm*)

This worm is not as common in English speaking countries as is the Tenia saginata. It is due to the eating of improperly cooked or raw pork. When fully grown it is from eight to twelve feet long and inhabits the small intestines, where as a rule it is solitary, though multiple teniæ are not uncommon. Its life history and other characteristics are best studied in works on pathology and diagnosis. It must be remembered, however, in connection with the *cysticercus* of the worm, that *it may in occasional cases lodge in one or more vital organs of man* and give rise to local changes and symptoms. To this I will again refer. The armed worm as a rule causes no serious symptoms and does not threaten life; the passage of the head is assurance that the host has been freed. If the head in its passage escapes discovery or if the proglottides are passed without the head, the host continues uncertain of the fate of the worm during several, usually three months; the time required for the development of the worm and the passage of its proglottides.

While the symptoms caused by the Tenia solium are not of serious import, the worm may by its presence interfere with stomach and intestinal functions, causing nausea, diarrhea, other symptoms of indigestion, including abnormal appetite, loss of flesh and mental torpor; with some anemia, all of which symptoms disappear with the passage of the worm.

The worm eliminates a poison which enters the blood stream and is directly responsible for the eosinophilia and anemia which are constant accompaniments of the tapeworm and of many other intestinal parasites.

The prognosis of the fully formed tapeworm as it inhabits the intestinal tract from the study of its life history and the preceding paragraphs may be said to be uniformly good and is readily influenced by suitable anthelmintics.

The deposit of the cysticercus in the brain may cause but few or no symptoms, in occasional cases the brain may tolerate the growth during long periods, depending upon the seat of the tumor caused by it; on the other hand it may threaten life by its presence and may cause the usual symptoms of a neoplasm. It may infest the base and cause pressure symptoms including paralysis of one or more of the cranial nerves. It may grow to considerable size, *causing destructive changes as it enlarges.* The *cysticercus racemosus* may lie loose in brain tissue, usually in the *ventricles of the brain.* In occasional cases *chronic basilar leptomeningitis* may be provoked. *Jacksonian and other forms of epilepsy, ependymitis and hydrocephalus internus, cerebral anemia and obliterating cerebral endarteritis* are mentioned by Askanazy as complications due to the presence of the cysticercus in the brain.

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The *cysticercus with its dense membrane* may continue to live in the tissues of man for years, may die, when calcification usually follows. The *skin* may harbor *cysticerci*, also the *muscular tissue*, the *liver, spleen*, the *intestinal wall*, the *heart*, the *lung*, the *pleura*, the *lymphatics* and *bone*.

The favorite seat of the cysticercus is the brain and the eye.

Cysticerci are not usually the cause of *local inflammatory changes or congestion*, neither do they give rise to marked sensory symptoms when in the skin.

In the eye, atrophic changes may follow (*phthisis bulbi*) (Askanazy).

(*b*) *Tenia saginata or mediocanellata*

Tenia saginata is the most common form of tapeworm in man; it is transmitted by the eating of infected beef, and grows to an average length of twenty (20) feet. This variety of tapeworm causes fewer complications than does the Tenia solium, may be carried without inconvenience in many cases, save the loss of the proglottides from time to time. In some cases there are colicky pains, indigestion, abnormal appetite and persistent malaise. Reckzeh reports the occurrence of *pernicious anemia caused by the worm. The cysticercus of the saginata is rarely imbedded in the tissues of man.* From 60 to 65 days lapse between the swallowing of the cysticercus and the appearance of proglottides in the stools.

The prognosis of Tenia solium is uniformly good. It occasionally happens that several trials must be made before the head passes, but full restoration of gastro-intestinal function to normal invariably follows the passage of the worm.

(*c*) *Bothriocephalus latus*

The bothriocephalus is the largest of all tapeworms, its *immediate host is the fish* almost always of the pike family and it is *distributed over Central Europe* (*Switzerland*) *and in Japan. In America* we occasionally find the worm in subjects who were infected abroad.

The bothriocephalus usually causes greater *gastro-intestinal disturbances* than do the other varieties of tenia; these include *diarrhea, persistent nausea, mental lethargy, depression and at times great irritability.*

In rare cases *convulsions* and other explosive nervous manifestations have been charged to the worm.

The greatest danger to the host is the development of *grave anemia which has all of the characteristics of pernicious anemia and is now considered by hemotologists to be identical with that disease.* (For the benefit of the student of the literature of *bothriocephalus anemia* I have appended the leading references on this subject from which in turn the full bibliography may be obtained).

It may be assumed in the light of our present knowledge that the dis-

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eased or dead bothriocephalus adds a poison to the blood stream which is hemolytic in its effect and causes the blood picture and constitutional disturbances of progressive pernicious anemia. Ehrlich, Biermer, Laashe and Schauman, the leading authorities on this subject have all reached this conclusion.

The prognosis of even advanced cases of bothriocephalus anemia is good, if the worm, dead or alive, is promptly expelled by treatment. *Full recovery is slowly reached.* Schauman proved that the *daily regeneration* of the *erythrocytes* after the expulsion of the worm varied between 60,000 and 214,000. In the beginning of the improvement he found the average midway between the extreme figures given; the *microcytes* disappeared early; *macrocytes* may at first be increased; later these disappear entirely and the normal blood picture is reestablished. This subject will be further considered in connection with *progressive pernicious anemia.*

(*d*) *Tenia echinococcus*

(*Hydatid Disease*)

The adult worm is not found in man. The worm itself is one-quarter inch long, occupies the intestine of the dog and wolf. The sheep is often the intermediate host. *In man, the cysticercus stage makes him an intermediate host.*

The six hooklets of the embryo set free by the digestion of the shell of the ovum, migrate through the intestinal wall and enter the blood stream or in some other way gain entrance to the brain, the liver, the spleen or other organs of the body. When the hooklets are deposited they disappear, and the embryo is slowly converted into a *cyst* of small size with two layers, one external or the *capsule*; the other internal or the *endocyst. The cyst wall encloses a light clear fluid.* The fluid of the cyst has an average specific gravity of 1010, neutral reaction as a rule; contains 98.5 per cent of water. Of the solid constituents sodium chlorid is in the ascendency. The albumin content is infinitesimal. The fluid contains a toxin which when injected into animals causes paralysis of the heart in diastole, lowered blood pressure and temperature. Soon there is a connective tissue enclosure which strengthens the cyst. *Daughter cysts* develop within the parent cyst and from these daughter cysts, other or grand-daughter cysts develop.

The echinococcus may live many years, or may die, when remnants of the original cyst are found within the fibrous wall in the invaded organs, calcified or otherwise changed.

Cysts may rupture and according to their location give rise to symptoms. Hydatid cysts are not frequent in America. In our practice we have seen but three. One we saw in 1878 at the Billroth clinic in Vienna (involving the neck, successfully removed) one in the clinic of Detmoldt

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in New York (liver echinococcus), and one of liver echinococcus which died, in our own practice. Lyon recorded 241 cases of hydatid disease in the United States and Canada "and several of these occurred amongst the Icelanders settled in Manitoba." Of the 241 cases 177 were in the liver; 26 in the omentum, the peritoneal cavity and mesentery. Eleven cysts were passed per rectum; in 7, the cysts or hooklets were expectorated and two escaped through the urethra.

The following statistical records taken from Allbutt and Rolleston show the incidence of echinococcus cysts in the various organs of the body:

In 1,000 autopsies at the Adelaide Hospital, South Australia, 49 bodies were found to contain hydatid cysts, i. e., 5 per cent. In 11 the cysts were multiple; in 5 two organs were infested; in 6 three or more viscera.

In 36 the liver contained a cyst.
In 9 the lung contained a cyst.
In 6 the spleen contained a cyst.
In 5 the peritoneum contained a cyst.
In 4 the brain contained a cyst.
In 1 the heart contained a cyst.

Thomas in 1,900 cases of hydatid disease found the liver infested in 5 per cent; the lung in 11.6 per cent; the kidneys in 4.7 per cent; the brain in 4.4 per cent; the spleen in 2.1 per cent; the heart in 1.8 per cent; the peritoneum, omentum and mesentery in 1.4 per cent.

The average of all statistics shows the liver to be the seat of the echinococcus disease in one-half of those infected.

Hydatid of the Liver.—There may be one or more cysts in the liver; the right lobe is the favorite location of these. The prognosis for life depends on the fate of the cyst, its location, size and the mischief which its presence causes.

Suppuration of Liver.—Echinococcus cysts may lead to grave constitutional and local disturbances, which unrelieved by surgical interference usually leads to death.

Perforation of hydatids of the liver may take place into one or more of several surrounding organs; into the *stomach; the intestines; the peritoneal cavity; the lung;* the bronchus; the kidney or into the portal vein. *Rupture* into the *lung or pleura* may lead to fatal *pneumonia,* to *gangrene,* to *empyema, sudden asphyxia, pyo-pneumothorax* and threatening *hemoptysis.*

With all perforations there is besides the local lesions great danger of *poisoning by the entrance of toxins from the fluid of the cyst.*

After aspiration of the cyst in many cases, distressing urticaria, also an evidence of toxinemia is frequent. Hence aspiration adds to the dangers unless operation follows immediately.

A large number of liver cysts remain latent during many years and the carriers die of intercurrent disease.

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Death may be caused by compression of the portal vein or toxinemia associated with obstruction of the bile passages.

Fistulous openings may result from the suppurating of liver cysts, and their burrowing to the surface; such patients unless relieved by surgical interference die from sepsis, emaciated and with the cerebral symptoms of toxinemia.

Spontaneous cure may follow perforation; not of sufficient frequency, however, to justify expectant treatment.

All operable cases of single liver echinococcus cyst offer a good prognosis. Multiple liver cysts are almost uniformly fatal.

Hydatid Cysts of the Lung.—Hydatids of the lung, as already stated, represent 11.6 per cent of those who suffer from echinococcus disease. Pleural invasion may lead to the symptoms and include the dangers of effusion, compression and its results. In many cases *encysted hydatids in the lung* do not threaten life; they may cause few or no symptoms. In other cases compression with inflammatory changes, cavity formation, *perforation,* occasionally *into the pericardium, septic fever* and *repeated hemorrhages* follow, with occasional *perforation into the pleura; empyema* and *pyo-thorax. Death follows lung hydatids in one-third of all cases.*

Hydatid of the Kidney.—*Echinococcus of the kidney* may be present without interfering with the health of the host during many years. They may be passed *per urethram* and without consecutive damage to the genito-urinary tract. In some cases the entire kidney is converted into a sac giving the physical signs and subjective symptoms of *hydronephrosis.* The prognosis is good, when, as a rule, the condition proves to be operable.

Rupture into the pelvis of the kidney is the usual fate of the cyst; this is followed by pyuria, fever and offers a good prognosis when radically treated. *Spontaneous recoveries are recorded after rupture.*

Kidney cysts may rupture into the peritoneal cavity, causing peritonitis; into the lung or bronchus, when the prognosis is unfavorable. The *external rupture of kidney hydatids* offers a good prognosis, the removal of the kidney with included cyst usually leads to cure.

Hydatid of the Spleen.—*This condition is rarely recognized without exploration, aspiration or post mortem.* Its surgical treatment is prompted and justified by the physical signs of enlarged spleen and persistent pain; when the prognosis is favorable. Unrelieved by surgical treatment the cyst itself, during long periods may not threaten life; it may, however, perforate into some one of the surrounding viscera and thus lead to serious complications and death. In rare cases sloughing and hemorrhage have followed and have caused death.

Omental, mesenteric and peritoneal hydatids present palpable tumors which are all operable and offer a good prognosis, better when the cyst is not broken during its manipulation thus preventing poisoning.

Hydatid Disease of the Brain.—*Intra-cranial hydatids* often grow to

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enormous size without causing symptoms. The cyst may be found either large or small in any part of the brain. Naturally *its symptoms and prognosis in most cases are those of brain tumor and depend upon its size and location.* Occasionally there are *multiple hydatids in the brain.* The cerebral hydatid is fourteen times as frequent as is the cerebellar (Sterling and Verco) growth.

Epileptic convulsions are a frequent accompaniment of hydatids of the brain; most patients die during an epileptic fit; they may fall into coma after a period of meningeal symptoms; they may live during a long period of paralysis, or, as often happens, they die of intercurrent disease.

Superficial hydatid cysts of the brain when localized by the diagnostician and attacked surgically, offer a fair chance of recovery.

Hydatids in the remaining organs of the body are so rare as to require no further consideration.

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2. Nematodes

(*a*) *Ascaris lumbricoides.* (*b*) *Oxyuris vermicularis*

The (a) *Ascaris lumbricoides*, and (b) the *Oxyuris vermicularis*, the most frequent of all worms, the former inhabiting the small intestines of

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children, the latter the colon, are without serious significance and promptly yield to the well known anthelmintics. Barring occasional febrile movement, irritability, petulance, rectal uneasiness, rarely reflex disturbances, such as convulsions, we have never found either of these round worms the cause of disease in our practice. Only rarely are distressing conditions caused by the *wandering of the ascaris.* Worms are vomited; at times they enter the postnasal space from the esophagus, the eustachian tube or the larynx. *Asphyxia* and *gangrene of the lung* are recorded among the accidents due to the wanderings of the worm (Osler). They may find their way to the liver, causing abscess, or to the bile ducts.

(c) *Ankylostomiasis*

(*Uncinariasis, Hookworm Disease, Miner's Anemia, Egyptian Chlorosis, Dochmiose, Ankilostomoanemia, Tunnel Disease*)

Ankylostomiasis is a form of progressive and grave anemia with symptoms referable to the gastro-intestinal tract and nervous system due to the Ankylostoma duodenale, originally described and recognized by Dubini in 1843.

The Papyrus Ebers, according to Scheuthauer and Joachim, about 3,550 years B. C. mentions a disease due to a worm Heltu which caused all of the symptoms of ankylostomiasis and has been known by the Egyptians from times immemorial. It is questionable whether the disease mentioned in the papyrus Ebers was identical with the present day hook-worm disease; Oefele denies it.

Occurrence.—The disease caused by the worm prevails in tropical and subtropical countries. On the Continent of Europe it is found among the miners of France, Austria, Hungary, Germany, Switzerland and Belgium. In England, the disease prevails among the Cornish miners (Boycott and Haldane) (Montgomery). In Egypt the disease is found among the natives and the Indian coolies. The credit for our exact knowledge of the hook-worm and its resulting disease as found in the United States belongs entirely to C. W. Stiles, whose conclusions are now fully accepted by the profession. (Full references to the contributions made by Stiles are given in the bibliography at the end of this chapter.)

The Infection.—The worm which causes the disease in the United States, it is now believed, does not belong to the Uncinaria but is given the name of the "New World Hook-worm or *Necator americanus of Stiles,* in contra-distinction to the "old world worm" or Ankylostoma duodenale. *Infection* is due to the development of the eggs, millions of which are passed with each stool of the infected patient. These develop in feces mixed with the earth or sand at a temperature of from 70° to 90° F. The human being is infected as a rule through the skin; from the fingers through the

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mouth, which latter method is unusual. Loos has demonstrated the course followed by the larvæ after entering the skin. They pass from the veins to the heart, into the lungs, through the pulmonary vessels, into the bronchi, and from there into the post-pharyngeal space to the esophagus and out through the stomach and intestinal tract. The lack of caution in caring for the infected stools is the paramount factor in the spreading of the disease.

The *"ground itch"* is prevalent among 90 per cent of those infected according to Ashford and King (H. W.).

Clinical Manifestations.—The leading clinical manifestations of hookworm disease include a period of malaise with increasing languor, after which gastro-intestinal symptoms predominate with circulatory and respiratory disturbances. The *anemia* is characteristic and is probably due more to the hemolytic action of the poison elaborated by the worm than by the direct loss of blood. *The red blood corpuscles* are reduced in proportion to the severity of the anemia from 1/4 to 1/10, the hemoglobin falls to 15 and 20 per cent in grave cases. It will be noticed that the color index continues high. *Eosinophilia* is a constant attendant, reaching as high as 40 per cent of all leukocytes in the more pronounced cases. Leukocytosis is rarely marked.

The complication of ankylostomiasis by pneumonia at once reduces the existing eosinophilia. Leichtenstern found a drop of eosinophils to 6-7 per cent from 72 per cent. Warburg from 65 per cent to 0 and a return of the eosinophilia with the recovery of the patient. Acute sepsis has the same effect.

Sufferers from the disease are lethargic; children continue dull and apathetic, they remain undersized, drag themselves about shiftlessly, and fail to attain their growth until years after puberty. The graver cases which continue unrelieved by treatment show the marked anemia, the faulty development, asthenia, dilated heart, respiratory embarrassment, the mental sluggishness, the skin changes of itch and the infected stools.

Incidence and Prognosis.—The incidence and prognosis of the disease have been enormously influenced by the education of the people which has resulted in concerted action to destroy the worm by removing the baneful conditions which make its multiplication possible and inducing the infected to care for themselves and to take advantage of specific treatment. The wearing of shoes to protect against infection through the skin has also been a powerful prophylactic factor.

Barring cases which have advanced to threatening asthenia with heart insufficiency and a blood condition which is extreme, the prognosis of treated cases is surprisingly good. In some cases there are relapses. The return to full health is often slow but certain. The blood is regenerated after varying periods.

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(*d*) *Trichocephalus dispar*

The *whip worm* or Trichocephalus dispar infects the large intestine of man. It is a small worm of peculiar build, with marked differences in the anterior and posterior parts of the body, being thin anteriorly and broad posteriorly; its length is from 4 to 5 cm.; the female is longer than the male.

The worm is not common in the United States but is frequent on the Continent of Europe.

Hundreds of worms may be present without causing symptoms or materially interfering with the health of the host. The prognosis is always good.

(*e*) *Trichinosis*

Trichinosis is an infection of man due to the eating of imperfectly cooked or raw pork or ham which holds in its muscle the *larval or encysted form of the Trichina spiralis.* The worm is a *nematode,* unusually resistant and infests the muscular tissue of man, giving rise to characteristic subjective and constitutional symptoms with a blood picture including *eosinophilia.* (Thayer and Brown.)

The Infection.—In the process of digestion the ingested larvæ are freed in the stomach; in 3 days the period of sexual activity begins in the intestinal tract. The sexes unite in the intestines and innumerable embryos are produced within from 7 to 9 days. The embryonic worm does not penetrate the intestinal wall as was formerly supposed, but the female

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worm finds her way from the muscular and mucous coat of the intestine by way of the lymphatics, the veins and the blood stream secondarily, to the striped muscles (mainly) of the host, in which they are easily recognized when bits of the muscle tissue are harpooned and examined microscopically. In occasional instances the *worm is encapsulated* within about 6 weeks. Nature finally provides the encapsulated worm with a dense *fibrous membrane* which, within from 4 to 6 months, becomes *calcarious*. In occasional cases, coincident with trichinosis, there are secondary infections which materially modify the course and the prognosis of the disease (cocci, etc.). The *encysted worm* may live undisturbed during many years.

Symptoms.—In most cases the infection is promptly followed by a *stage of intestinal symptoms.* These symptoms vary in accordance with the severity of the infection. *In the severer cases, diarrhea, colic and vomiting are in the ascendency; all severe and exhausting. The mild cases* may present none of these intestinal manifestations; on the other hand, there are *severe cases in which the early symptoms of intestinal invasion are not outspoken at once*, but these symptoms gradually develop or may be entirely absent.

In all cases the prognosis is largely influenced by the number of the invading worms. Grave symptoms often follow before the embryonic worm has had time to settle in the muscular tissues of the patient. These symptoms, including great exhaustion and muscular weakness, are due to the poisoning influence of the worm (metabolic products of the trichinæ themselves), for it has been proved experimentally that the blood serum of the trichinous animal is poisonous early, i. e., before muscle invasion.

The prognosis, after muscular invasion, depends, besides, upon the resistance of the patient, the degree of constitutional disturbance, the extent and location of the muscular invasion, the severity of the nervous manifestations and the gravity of the complications.

Marked muscular rigidity and severe and widely spread muscular pains, with high fever, rapid pulse, albuminuria, diarrhea, delirium, the Kernig symptom following the period of intestinal symptoms, and evidences of *edema of the glottis* are among the more serious manifestations of trichinosis and demand a guarded prognosis.

Involvement of the respiratory muscles, including invasion of the muscles of the larynx and diaphragm, associated with *hoarseness and dyspnea*, at times *marked air hunger and cyanosis*, is always alarming and is present in the graver forms of the disease and demands great caution in offering a forecast.

When the *constitutional symptoms* include a long-continued *typhoid condition* with *increasing weakness* and *emaciation*, and an *unfavorable blood picture*, the prognosis remains doubtful and grave during several days.

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The presence of *albuminuria* with other favorable symptoms is not of serious import.

The presence and persistence of the *Diazo-reaction* does not influence prognosis.

Bronchitis is a frequent and not a serious complication when limited; when the smaller tubes are invaded and there is also *respiratory embarrassment* due to muscle disturbance (diaphragm, etc.), the bronchial catarrh may add an element of danger and cloud the prognosis.

When *myocardial weakness* is present sufficient to cause *edema of the extremities* and other evidences of *heart insufficiency*, unless the disease has run its course or the heart responds to treatment, the outlook is exceedingly grave.

Pneumonia, whether lobar or lobular, is always a grave complication; this is the rule in those cases in which respiratory symptoms due to trichinosis already exist and the dyspnea is associated with a feeble and non-dependable circulation.

Limited peripheral thrombosis, when without other serious complication, adds but slight danger to the disease. *Cerebral thrombosis or thrombosis of other vital organs* is almost always unfavorable.

In the chronic cases, those dragging along during several months, the development of *bed-sores* retards recovery and may lead to secondary infection.

Enlargement of the spleen is in all probability due to secondary infection, its disappearance is always to be interpreted favorably. During the first two weeks of the disease the spleen offers no prognostic data.

Blood.—The blood shows characteristic changes which demand its close inspection for diagnostic and prognostic purposes. The *red blood corpuscles* show no marked change. *Leukocytosis* in mild cases is not excessive. *The more severe cases show a decided tendency toward polymorphonuclear leukocytosis.* There is an *enormous increase of eosinophils with displacement of neutrophils.* This may mount to from 30 to 60 per cent. (Thayer and Brown.) Staubli and Hegar claim that *in spite of the relative reduction of the neutrophilic leukocytes there is an absolute and marked increase of these*, sometimes reaching as high as three times the normal count and therefore the high eosinophilia is not present at the expense of the neutrophils. It has been shown that as a rule *the graver forms of the disease are associated with the highest eosinophilic counts.* Schleip found percentages varying in accordance with the gravity of the disease, between 20 and 62 per cent. Kerr found 86 per cent in one of his cases. Thayer and Brown found 16,000 eosinophils (in 1 c. mm.) as against the normal count of 150-250.

Moderate eosinophilia may persist long after convalescence, and *in occasional severe forms of the disease may be limited and insignificant.* Improvement usually follows the appearance of moderate *lymphocytosis*

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and a striking increase in the number of blood-platelets. Eosinophilia is not likely to be marked during the stage of intestinal invasion, but depending upon the metabolic products of the Trichina spiralis, is coincident with the deposit of the worm in the muscles of the body.

The *duration* of *mild cases* is from 16 to 35 days. The *severe infections* may continue during several months; these cases are followed by a slow convalescence, long periods of muscular weakness, asthenia, myalgic pains and occasional intestinal anomalies.

Most deaths occur between the third and fifth week of the disease; in over 60 per cent of these, there is invasion of the respiratory muscles and often *secondary bronchopneumonia.*

Owing to a guarded quarantine and the thorough examination of pork and its products, trichinosis is at present comparatively infrequent.

Mortality.—The mortality varies in different epidemics and is influenced by the factors already considered. I have in my experience found the mortality of our hospital cases low. The average mortality may be placed between 4 and 30 per cent. *Children* bear trichinosis much better than do adults.

It must be remembered that rheumatic pains and vague symptoms may continue during many years.

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(*f*) *Filariasis*

There are a number of round worms belonging to the family *Filaridæ,* which infect the blood of man or other portions of the body, discovered by Wucherer, 1866, in Bahia and by Lewis in 1872 (*Filaria sanguinis hominis*), which give rise to symptoms. Most of these worms pass during the night from the lymphatics into the blood stream. The leading symptoms caused by these nematodes are *hematuria, chyluria, elephantiasis, lymph-scrotum, chylous ascites and elephantoid fever.*

The blood filariæ which interest us are:

a. Filaria Bancrofti (Cobold, 1877).
b. Filaria diurna (Manson, 1891).
c. Filaria perstans (Manson, 1891).

The filaria of Bancroft causes *hematocyturia* and the *lymph-scrotum.* The blood shows the presence of the worms during the sleeping hours,

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whether the patient sleeps during the day or night. The blocking of the lymph-channels causes most of the conditions already mentioned and *elephantiasis.*

All of these conditions may persist during many years without causing marked inconvenience or affecting health.

The *lymph-scrotum* may lead to great inconvenience because of its size, the *thickening of the skin* and the *change in the lymphatics,* but it is not directly dangerous to life.

There are cases of *filariasis* in which there are a number of weeks or months, occasionally years, of *lymphangitis* with *erysipelatous inflammation and fever.* (*Elephantoid fever.*) *Abscesses* may develop in these cases; surgical treatment has relieved some of them.

The prognosis of *scrotal elephantiasis after amputation* is good; occasionally recurrences have followed cases in which the incision was made in diseased tissue.

In women, the infection may produce *elephantiasis of the external genitals, and the mammary glands of both sexes may show enormous enlargements.* With persistence of *chyluria* and *hematochyluria* patients may live undisturbed during many years.

Occasionally anemia causes weakness and threatens life. Only rarely does the patient die without intercurrent disease.

Spontaneous cure can only occur in the most favorable surroundings where fresh infection can be prevented.

3. Trematodes

(*Bilharzia hematobia—Bilharz*)

The blood fluke (Schistosomum hematobium) or Bilharzia hematobia was first recognized by Bilharz in 1851. The male worm is one-half inch long, the female three-quarter inch. The adult worm carries the female in a curved canal (gynecophoric canal). The worm is found mainly in Northern and Southern Africa, in Persia, Arabia and along the west coast of India. Griesinger in 1851 called attention to the frequency of the worm in Egypt, where in 363 autopsies bilharziæ were found in 117.

The leading inconveniences caused by these blood flukes are *hematuria, bladder and kidney irritability, consecutive cystitis and secondary anemia.* There are in some cases rectal and vaginal disturbances leading to *tenesmus and dysenteric symptoms and chronic vaginitis, due to direct local infection.*

Among the *complications* which materially influence prognosis are *profuse hematuria with secondary anemia, pyelitis, nephritis, renal and bladder calculosis, dysentery, asthenia and marasmus.* In *some cases the*

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low hemoglobin content of the blood is characteristic with a relatively high red blood corpuscle count (*oligochromemia*). There is some leukocytosis (40 per cent) (Grawitz). Lymphocytes and eosinophils reach as high as 53 per cent.

The gravest forms are found in men oftener than in women.

Multiple urinary fistulæ often complicate bilharziasis very materially and unless relieved may lead to septic conditions or tend to drain and exhaust the patient. Even the grave forms of bilharziasis do not run an acute course but in the overwhelming number of cases are chronic, covering years, and patients may die of intercurrent disease besides the complications already mentioned.

Liver flukes are rare in America or on the Continent of Europe. In Japan, China and India, they are found infecting the *bile passages, causing enlargement of the liver, icterus, pain, gastro-intestinal symptoms* and in the *terminal stages dropsies and ascites with marked anemia.* The disease is chronic and usually causes death.

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E. Infections of Unknown and Doubtful Origin

I. Poliomyelitis

1. Acute Anterior Poliomyelitis

(*Infantile Paralysis, Heine-Medin Disease:* 1840-1887)

The revelations of the past fifty years have led the pathologist and clinician to positive views concerning the various forms of poliomyelitis, and justify a definition which proves the infection to be far-reaching in its effects, by no means limited to the anterior multipolar cells in the cord, in which by predilection, it is true, the greater changes are produced and are promptly recognized. To the reader who is eager to study the history of the disease, we would commend the references appended to this chapter.

Our present conception of infantile paralysis justifies the conclusion that it is an infectious disease of early life, as a rule communicable. In all probability it is due to a filterable organism which is ultramicroscopic, causing a short period of indefinite symptoms followed by the prompt development of paralysis in most cases, and other features of invasion

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of the nervous system; these depend entirely upon the location and extent of the lesions. The clinical types are numerous and well defined, making localization and accurate pathologic conclusions possible.

It is not at all unlikely that the minute organisms found by Flexner and Noguchi, consisting of globoid bodies 0.15 micron to 0.3 micron in diameter, and arranged in pairs, chains or masses, are the true cause of the disease. This question is still *sub judice.* Flexner and Noguchi have grown the cocci in human ascitic fluid. They pass through the Berkefeld filter, are capable of reproducing the disease in the monkey, and from these they can be again recovered in pure culture. The organism is anaërobic.

When the clinician for either diagnostic or prognostic purposes considers the underlying pathologic changes of anterior poliomyelitis, he must remember that he is dealing with an infection in which all structures of the nervous system may be involved, with a strong preference for the motor neuron. Hence to focus our attention upon the structures most prominently included in the pathologic picture, we consider the various manifestations of the disease as expressions of either neuritis, acute anterior poliomyelitis, meningitis, meningomyelitis or poliomyeloencephalitis. Occasionally the paralysis is of the Landry type, to which we will again refer. The above conclusions are corroborated by a study of the epoch-producing contributions to the literature of this subject by Heine, Medin, Wickman, Strumpell, Bergenholtz, Flexner and Römer. Clinical and pathological material thoroughly studied, is convincing. The fact which we wish to impress is that *so-called anterior poliomyelitis can no longer be considered to be a disease of the anterior horns alone, but that its pathology and symptomatology may include changes in the central and peripheral nervous system as well as in the membranes of the cord and brain, in a large number of cases.*

The disease is now more frequent than ever before, and is also spread over a larger territory. Rosenau in the following table shows the number of outbreaks and the number of cases from 1880-1910:

	Cases.	Outbreaks.	Average Number of Cases per Outbreak.
1880–1884	23	2	11.5
1885–1889	93	7	13
1890–1894	151	4	38
1895–1899	345	23	15
1900–1904	349	9	39
1905–1909	8,054	25	322

Of the 8,054 cases reported between 1905 and 1909, 5,514 or about five-sevenths were found in the United States.

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The cases have been more severe during the past few years than ever before, and in certain sections the number of ascending paralyses in adults, of the Landry type, have been correspondingly frequent and fatal. A further interesting feature is the greater fatality and relative frequency in the country districts and small villages than in the crowded cities. It has been my experience that outlying districts of cities, and sparsely settled sections, offer more cases than do central and thickly populated centers of cities. The majority of cases occur during the warmer months of the year; while sporadic cases are found regardless of season.

It is not within the province of this work to consider the port of entry of the infecting agent: the consensus of opinion favors the nasopharyngeal route. We might add, however, that in our last case, which was severe and of the bulbar type, the disease followed within six days after the bite of a large horsefly, in a child four years of age. (See Rosenau.)

It is further to be remembered that the disease may be conveyed by *"healthy carriers"* who harbor infecting material in their nasal secretions —a fact which Flexner, Clark and Fraser have proved experimentally. There are no positive proofs that the disease is not directly contagious and in the present state of our knowledge, including the larger experiences of the Swedish observers, it is safe to so consider it. The *period of incubation* may be placed at from eight to ten days, with an average of seven days.

The Prodromal Period.—The prodromal period offers practically no positive prognostic data. There are cases in which the pulse is rapid and feeble from the beginning and in which the disease proves grave, often of the bulbar type.

The *temperature and pulse* taken together during the prodromal period are not to be relied upon for prognosis. Early involvement of the respiration, rapid and superficial breathing during this period is always significant and is found with the bulbar type of paralysis, or may be due to *bronchopneumonia*, which is a frequent cause of death.

Gastrointestinal symptoms are among the most frequent accompaniments of the first stage of the disease; they are controlled or yield spontaneously in most cases.

The *blood examination* in this stage may be of great diagnostic and prognostic value, for it shows marked *leukopenia.*

The *nervous manifestations* of the prodromal stage include more or less *somnolence without psychic disturbances. Drowsiness and stupor* during the early stage of the disease are not of unfavorable significance, and are more favorable than alertness. This experience was confirmed by the results of the investigations made by Draper of the Rockefeller Institute.

In very young children *convulsions* need not be interpreted as serious; often they are followed by the stage of *paralysis* and other symptoms,

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which at once clear the horizon, making the diagnosis of the disease and its type possible, and often permitting of a tentative but not a positive prognosis.

The pains and rigidity during the prodromal period are in proportion to the extent of the meningeal infiltration (*leptomeningitis*).

Profuse perspiration is usually present in both severe and mild cases.

It is impossible to gain accurate diagnostic or prognostic data during the early stage, for as Römer has well said, "the initial symptoms are not characteristic of any one type of disease, but they are conglomerate, with the possible prominene of one symptom referable either to the meninges, the gastro-intestinal tract, the respiratory organs; or the features of influenzal fever may predominate." This period is usually short, from twelve hours to three to seven days, and is followed by the second stage, *the stage of paralysis.*

Stage of Paralysis.—*It is in the stage of paralysis that we recognize the nature and the type of the disease. The diagnosis cannot be positively made before the appearance of paralysis; during endemics it can only be suspected.*

We recognize the following types (Römer):

(a) Abortive
(b) Spinal
(c) Landry
(d) Bulbar and pontine
(e) Cerebral
(f) Ataxic
(g) Polyneuritic
(h) Meningeal

(a) Abortive Type.—Wickman's statistics showed that of 1,028 cases thoroughly investigated by him, 157 were of this type (15.3 per cent). In these the prognosis is uniformly good. *The toxins in this type do not attack the motor neuron nor the other central organs, and there is therefore no paralysis.*

The features which are prominent and yield after a few days are fever, pains in the head and back, tonsillar invasion, bronchitis and all of the other manifestations of the prodromal stage of the more severe cases.

Edward Müller has described cases which offer a good prognosis, in which there are *transitory paralyses of a single group of muscles,* or there may be *evanescent loss of the tendon reflexes.* These he has characterized as *"rudimentary poliomyelitis."* Müller places the incidence of the abortive types much higher than does Wickman. The former claims that during epidemics fifty per cent of all cases are of this type. My experience proves that not all epidemics are alike in their virulence, and we have often found the coincidence of other acute infections with infan-

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tile paralysis, which may have been considered abortive forms of the disease, and which may account for these varying conclusions. The larger number of abortive cases were found between the ninth and eleventh year, and during this period it will be noted from the study of Wickman's tabulation, there are the fewest paralyses.

(b) SPINAL TYPE.—The spinal type is the most frequent of all forms. The paralyses are promptly evident *"paralysis of the morning."* It is a *complete motor paralysis.* It soon proves to be flaccid; it may in some cases be extensive, involving all four extremities; it may be irregularly distributed, or it may from the beginning limit itself to one group of muscles. When two or more extremities are paralyzed, one extremity usually suffers more than do the others. The peroneal and quadriceps muscles are oftenest involved and permanently damaged. The cranial nerves including the ocular apparatus are only rarely involved; neither are there sphincter paralyses. *Sensory symptoms* are due to associated cellular infiltration of the meninges or the sensory tract, and are of short duration as a rule. *Muscular atrophy* is the fate of the muscles which remain paralyzed; with the flaccid paralysis the *reaction of degeneration* is present.

The reaction of degeneration does not argue against the possibility of final restoration of function. Its persistence without motor improvement from six to twelve months after the onset, leaves but little hope for cure of the remnant of paralysis.

With the atrophy of the paralyzed muscles there are *trophic changes. The more developed the latter,* including shortening of the affected extremity, interference with the bone growth, marked and persisting lowering of the local temperature, *the less favorable are the chances of restoration of function.*

Persistence of changed deep and superficial reflexes is unfavorable; in these cases the paralysis is likely to persist though the education of accessory muscles may prove of great assistance.

Urinary retention during the prodromal period or following, is not, in the spinal form, an unfavorable symptom. We have found it both in the adult and in early life. In young boys (2-6 years) the urethra is not infrequently plugged with a dense phosphatic deposit, which is likely to recur, but is not unfavorable.

Consecutive contractures remain and can only be overcome by orthopedic treatment. *Equinovarus* is the characteristic contracture which remains when the lower extremity is paralyzed.

Resulting deformities such as *kyphosis* and *scoliosis* may often be prevented by proper treatment. When developed, they are likely to remain, though in rare cases modern methods of mechanical treatment may result in marked improvement. In rare cases there may be exacerbations with fresh paralyses which are not usually extensive and are likely to disappear.

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(c) Landry Type.—Our experience justifies the conclusion that Landry's ascending paralysis is identical with poliomyelitis, there being two forms of the disease.

In the *first form* there is the characteristic and prompt development of ascending paralysis, usually beginning in the lower extremities, ascending, and in the course of three to five days involving the diaphragm and respiratory muscles; finally there is the pneumogastric and glossopharyngeal; with spasm of the glottis, air hunger and death, usually before the end of the seventh day. The majority of patients die between the third and fifth day of the disease. Schluckpneumonia (aspiration) is not uncommon.

In the *second form* we have during the first twenty-four hours recognized the ascending paralysis. The respiratory muscles are less involved; the upper extremities are paralyzed before the end of the fourth day; but the pneumogastric and glossopharyngeal are not involved in the process. The patient may live and continue paralyzed. Such cases are rare but they do occasionally present. We saw a student with this complex of symptoms ten years ago, who has since entered the practice of law in which he is making a brilliant success in spite of the motor paralysis of his four extremities, which has remained unchanged.

(d) Bulbar and Pontine Type.—The bulbar and pontine form of poliomyelitis was described by Medin and includes the involvement of the cranial nerves in the motor paralysis. As a rule the bulbar and pontine invasion is coincident with the spinal form of the disease, as in a case (age four) at present under observation, in which there is paralysis of both lower extremities and both arms—the left greater than the right—and in which during the first four weeks the left facial nerve was also included. In this case the facial paralysis has disappeared (six months) with marked improvement of all other paralyses. The *facial is oftener paralyzed than any of the other cranial nerves.* The abducens and motor oculi are rarely included. Our material includes one case in which the optic nerve was involved.

(e) Cerebral Type (*Polioencephalitis*).—These forms of the disease are a *mixture of poliomyelitis and encephalitis* and were originally described in a brilliant article of Strümpell, whose observations have since been verified by Medin. The characteristic cerebral paralysis includes hemiplegia in children with marked trophic changes, developmental anomalies, contractures, accompanied by the usual adduction of the arm, with flexed elbow and well marked clubfoot (pes equinovarus). *The reflexes* in children with these symptoms are likely to continue abolished; in the adult they may be present or exaggerated; Babinski persists or may be absent. In children *athetosis* may finally develop.

Cerebral polioencephalitis may involve the cerebellum and its paths. The paralyses due to this form of poliomyelitis may improve, but com-

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plete return of function cannot be expected. The majority of these children remain bright, but go through life hemiplegics.

(f) Ataxic Type.—Medin, Wickman, and Zappert observed symptoms in some of their cases which after the prodromal period resembled *Friedreich's hereditary ataxia.* In these cases the prognosis for full restoration of function is unfavorable.

(g) Polyneuritic Type.—These cases present all of the features of multiple neuritis. They arise during epidemics of the more common forms of poliomyelitis, and are held by Medin to be due to the same virus which causes all other types. They are associated with sensory symptoms and tender nerve trunks; there are often evidences of meningeal inflammation, including the Kernig symptom. The prognosis of the polyneuritic type of the disease is favorable, though recovery may be slow.

(h) Meningitic Type.—In this form of the disease there are, during the early days, many of the symptoms of acute leptomeningitis arising in the midst of an epidemic of poliomyelitis, including the *Kernig symptom.* This is followed in most cases by well developed paralyses with the usual characteristics of infantile paralysis. Netter reports that twenty-nine per cent of his cases are of the meningitic type of the disease.

General Considerations

Lumbar Puncture.—In the *fatal cases of Landry's ascending poliomyelitis* the fluid escapes under high pressure and contains albumin in appreciable quantity. There are no polymorphonuclear cells but the French have confirmed the observations made by some American observers that there are a good number of lymphocytes present.

In the *usual forms of the disease* the fluid escapes under moderate increase of pressure, the quantity of the fluid being increased; it is usually clear, contains no microörganisms, and gives a negative Wassermann reaction. For both prognostic and diagnostic purposes it is of interest to note that while the withdrawn spinal fluid continues negative, the blood (as reported by Plaut and Schottmüller) is likely to give a positive Wassermann reaction during the acute period, and becomes negative at the end of four weeks—with the improvement of all symptoms. The globulin reaction is positive, according to the experience of most clinicians, though in the recently published work of Plaut it is claimed to be absent. Lmphocytes are present in the fully developed cases in the fluid.

Electrical Reactions.—Oppenheim believes that the electrical response of the paralyzed muscles gives important prognostic information. Those muscles, he claims, in which the *reaction* to the *faradic current* is not entirely lost after the third week will be likely to recover full power ultimately.

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Groups of muscles in which at the end of the first week of paralyses there is *complete reaction of degeneration* are not likely to recover in the majority of cases, though the prognosis is not bad in all of these, as has already been indicated. We have seen full return of power with both complete and partial reaction of degeneration. Eckert believes that inability to move the toes is unfavorable for the full restitution of motor power in the paralyzed leg.

Conclusions.—A study of the preceding pages must lead to the conclusion that *poliomyelitis is not an innocent disease; that deaths are not infrequent as the direct result of the infection*—a fact which is not surprising in the light of our present conception of its pathology. The most convincing conclusions must rest on the study of a large number of cases cautiously investigated. This has been conscientiously done by Wickman (Governmental investigation, 1905) in 1,028 cases. Of these 868 were paralyzed, 157 were abortive cases (15.3 per cent) and showed no paralysis, or only transitory motor symptoms. Of the entire number 159 died (12.2 per cent). The average number of days these lived was fifteen. Following the cases paralyzed which finally died, we find that by adding these to the early deaths, *the mortality of poliomyelitis was* 16.7 *per cent. The mortality varies in different epidemics from ten to forty-two per cent.* The mortality as given by nine collective investigations (Römer, page 27) was between 10.8 per cent and 22.5 per cent. In the monkeys infected experimentally the mortality is very high, 75 to 76.4 per cent (Römer, Flexner and Lewis).

Of Wickman's 157 deaths, 14 died after the fifteenth day and 143 between the first and the fifteenth day. The following table (Wickman) proves that the fourth day claims the larger number of children (25.5 per cent).

Table showing number of deaths between the first and fifteenth days of the disease inclusive:

Died	on	1st	day	of	disease	.....	1
"	"	2d	"	"	"	.....	6
"	"	3d	"	"	"	.....	22
"	"	4th	"	"	"	.....	36
"	"	5th	"	"	"	.....	25
"	"	6th	"	"	"	.....	15
"	"	7th	"	"	"	.....	16
"	"	8th	"	"	"	.....	3
"	"	9th	"	"	"	.....	5
"	"	10th	"	"	"	.....	7
"	"	11th	"	"	"	.....	2
"	"	12th	"	"	"	.....	1
"	"	13th	"	"	"	.....	2
"	"	14th	"	"	"	.....	1
"	"	15th	"	"	"	.....	1

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The following table taken from Wickman's report of his collective investigation proves that adults are not exempt from the disease and that the death rate is higher in adults than in children:

Table showing ages, number paralyzed, number of abortive cases, number of deaths during first fifteen days, and mortality in per cent of paralyzed cases.

Age, Year.	Cases with Paralysis.	Abortive Cases.	Died During First 15 Days.	Mortality in Per Cent. of the Number of Paralyzed Cases.
0– 2	169	14	17	10.
3– 5	181	33	21	11.6
6– 8	154	25	23	14.9
9–11	88	35	10	11.4
12–14	77	29	22	28.6
15–17	59	8	14	23.7
18–20	53	5	15	28.3
21–23	24	3	8	33.3
24–26	14	1	3	21.4
27–29	11	1	3	27.3
30–32	12	2	4	33.3
33–35	3	0	0	0.
36–38	10	0	1	10.
39–41	6	0	2	33.3
41–44	0	1	0	0.
45–47	2	0	0	0.
48–50	1	0	1	100.
51–53	1	0	0	0.
54–56	2	0	1	50.
65	1	0	0	0.
	868	157	145	....

There were 592 cases with 71 deaths in children between 0-11 years of age (mortality of 12. + per cent), whereas between the 12th and 32d year there were 250 cases with 69 deaths (mortality of 27.+per cent). In one case the father of nine children (all in the same house) contracted the disease without a single infection among the children.

If children live beyond the 15th day the chances are that life will not be longer threatened. Children living beyond the 7th day are not likely to die.

Twenty per cent of all paralyses recover fully, according to Neuroth. Wickman claims in children from 9-11 years, 48.4 per cent; after 11th year 32.2 per cent. Leegard's figures show children to the 14th year, 30.4 per cent, and after the fourteenth year 22.2 per cent of recoveries from paralyses.

We are justified in concluding that poliomyelitis leads to death in a larger number of cases than has been heretofore supposed; that the prognosis for life therefore must be guardedly given until beyond the

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first week; that paralyses which are well developed may yield; that in the larger number of paralyses remnants will remain; that paralyses which persist beyond six to twelve months will prove to be permanent, with but slight modification; that trophic changes persisting beyond twelve months remain uninfluenced; and that the most fatal form is the ascending type with symptoms of Landry's disease.

So-called sporadic cases offer an excellent prognosis so far as the life of the patient is concerned, though the paralyses are more likely to be permanent than are those of the epidemic types.

Cases of human and experimentally produced poliomyelitis prove that the length of the period of incubation offers no positive data for prognosis.

2. *Chronic Poliomyelitis*

There are a number of cases of unknown origin occasionally following trauma, in which there is a subacute or chronic course with paralysis, closely resembling the spinal type of the acute disease. These cases are found in adults without the acute period of the epidemic forms and resemble, when fully developed, the spinal type of muscular atrophy. They differ from progressive muscular atrophy because of *the early paralysis and the atrophy which follows it.* There may be *exacerbations during which further paralysis develops,* involving separate groups of muscles in which atrophy follows, with the flaccid paralysis. There is *loss of reflexes* and the *reaction of degeneration.*

In occasional cases there may be marked improvement of all symptoms. In a number of cases the exacerbations lead to *progression of the atrophy,* and with *ascending symptoms* and increasing weakness the patient dies. These cases represent degenerative processes in the anterior horns, are often difficult to differentiate from *progressive muscular atrophy,* though as already mentioned, the early flaccid paralysis offers a differential feature. The *atrophic changes are secondary,* never primary. The *lower extremities* are usually involved first, though there may be *monoplegia,* and later extension to other parts.

The prognosis so far as life is concerned is less favorable than progressive muscular atrophy, for the disease when progressive, ends fatally in from one to four years.

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II. Scarlet Fever

(*Scarlatina,* Ger. *Scharlach*)

Scarlet fever is an acute infectious contagious disease, of unknown origin, and of early life, characterized by fever, a far-reaching (scarlatinal) erythematous eruption, usually followed by desquamation and associated with throat complications of varying intensity, lymphatic enlargements and a strong tendency to sequelæ in which the kidney, heart and joints may suffer serious damage. Children between 3 and 8 years of age are most disposed to scarlet fever; resistance seems to increase with increasing years.

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In considering prophylaxis and prognosis, let it be remembered that the disease is contagious until the end of desquamation and one or two days before the outspoken symptoms of the disease. The corpse also holds and spreads the infection. The so-called "mild scarlet fever" may spread the infection and cause malignant disease in others. There are cases of scarlet fever without rash and with slight tonsillitis. It is exceedingly difficult, in fact *impossible, to offer any forecast of value during the early days of the disease,* save in those cases which may be recognized at once as *malignant,* in which the duration is short and death prompt, often before the rash has appeared. There are so *many and such serious complications* which may influence the course of scarlet fever, *whether the initial symptoms are mild or severe,* that it is never wise or safe to offer a forecast which commits the physician. Cases beginning with mild symptoms may be finally complicated with serious organic diseases of vital organs, while it is not at all uncommon to find those with alarming symptoms during the first five or six days of the disease march to complete recovery without an untoward incident. It is safe to consider *those cases gravest,* in which, during the period of invasion, there are *marked cerebral symptoms, much vomiting, rapid pulse, high temperature and suppressed urine with albumin in the little that is voided.*

Occasionally a case presents with symptoms so grave during the *period of invasion,* including those of profound and sudden *sepsis,* with immediate *heart weakness,* that death results before the appearance of the rash. These cases are not so frequent as formerly; it is a question whether the nature of the infection has not been influenced favorably by some unknown factor, for those who practised during the dark days of "malignant scarlet" and "masked scarlet fever" have lived to repeat these experiences only at rare and long intervals. Those were the days when entire families of children were stricken and died within twenty-four hours. In Central New York thirty years ago these experiences were frequent; I know of no repetition within the last twenty years in my own or in the practices of my colleagues, though now as before *it is clear that the mortality varies in different epidemics and in different countries from* 3 *to* 50 *per cent.* The highest mortality has been found during October and the winter months. The depth of color of the eruption varies, but experience teaches that *early mottling of the skin, cyanosis, purple-tinted, purpuric, or hemorrhagic* eruptions are strongly suggestive of severe infection, offering *unfavorable prognosis in direct proportion to the degree of myocardial weakness. Widespread deposit on tonsils, pharyngeal wall and uvula,* membranous in character, *diphtheritic or streptococcic,* is proof of mixed infection, and should lead to a guarded prognosis.

Considerable *involvement of the cervical lymphatics,* with widespread angina, is found with the more severe infections, and should be given considerable weight in offering a forecast.

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If with *pharyngeal and cervical invasion the nasal mucosa is also involved,* and the symptoms of general infection manifest, more particularly, *if the heart is showing evidences of added burden,* the prognosis becomes grave. These cases are usually *diphtheritic* and reference to them will be repeated. *Termination of the febrile period by crisis* is in the majority of cases favorable.

What complications may follow in any of these cases no diagnostician can foresee. *Increase of symptoms,* including great *unrest, somnolence, delirium, persistent vomiting, between the second and fourth days of the disease, with deepening color of the eruption, cyanosis, with or without tonsillar change,* but with *increasing rapidity of the heart action* and *dilatation of ventricles is of grave import* (Toxic scarlatina) (Schick).

Diphtheritic Infection.—*Necrosis,* sloughing of tonsillar tissue with symptoms of grave diphtheritic infection (positive bacteriologic diagnosis), between the 3-5 days of the disease, often with *middle ear and nasal* invasion, is found in the graver forms of the disease. If the *sloughing* is deep, and, as individual sloughs are cast off, there is no tendency to heal, the prognosis is more serious than in those cases in which, as often happens, the slough (i. e., process of necrobiosis) is superficial with prompt healing, decrease in size of lymphatics and constitutional disturbances.

Persistent high temperature without decided fall during the morning hours with sloughing, is indicative of *deep infection* and is *serious.*

The *depth and extent of destruction of pharyngeal tissue* are important factors in prognosis. *Extension* to the *larynx* with widespread pharyngeal *destruction is serious,* as is also *laryngeal croup. The lower the temperature on the second day of the disease* (eruptive period) in cases remaining uncomplicated, the more favorable is the prognosis.

The Ear.—The ear offers important data for prognosis; *its early infection* in cases with symptoms of *spreading infection* (particularly *diphtheria*) and associated deep *necrosis* of tissues, is always serious. Acute otitis causes increase of temperature, interferes materially with nutrition and may lead to acute meningitis from mastoid invasion or may be the cause of sinus thrombosis, with its serious accompaniments.

Chronic changes may follow early or late *otitis media suppurativa,* causing *deafness, spreading infection, pyogenic disease of the brain,* months and years after the initial disease.

Chronic mastoiditis with latent abscess continues to be a menace and may remain unrecognized, to be suddenly lighted into activity, and may cause meningitis and death.

Otitis suppurativa may spread infection to distant organs; the pericardium, endocardium and joints have been infected by pus producing organisms from this source.

The Respiratory Organs.—*Pneumonia* (staphylococcus or streptococcus) secondary to otitis has followed with serious results in many cases.

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Purulent pleurisy (*empyema*) dependent on otitis is always a grave complication.

A very large number of middle ear suppurations are late complications, often during convalescence, which, when recognized early and radically treated, offer a very favorable prognosis.

The Blood.—There is a moderate *leukocytosis* and *eosinophilia* with scarlet fever; a decided drop or absence of the latter is unfavorable. Reckzeh reports that leukocytosis and eosinophilia are at their height as the eruption begins to fade.

The Cardiovascular System.—*Children bear a rapid pulse well during the early stages of scarlet fever*, hence rapid heart action without evidences of dilatation or myocardial weakness, secondary cyanosis or mottling of the skin, is not of itself serious. *Persistently rapid heart action* (140 and above) *is usually* evidence of profound infection and grave.

Small, thready, rapid pulse, above 150 *on the first day, in children,* with other grave symptoms is always ominous.

Acute myocardial degeneration with dilatation is promptly shown in symptoms of circulatory insufficiency, congested skin, cyanosis, dyspnea, and is among the serious complications whenever present. *Endocarditis* (acute) *and pericarditis* are frequently associated with myocardial degeneration.

Scarlatinal endocarditis is, next to rheumatism, the *most frequent cause of chronic valvular disease.* When *acute endocarditis* and *nephritis* are *co-existent,* as often happens, the prognosis is less favorable than if but one of these complications exists. Many cases, however, recover and it is surprising to find among these but scant remnant of disease in either heart or kidney if patients are cautiously watched and scientifically treated. To improve the chances of scarlet fever patients, the endocardium demands the same watchful care in this disease as in rheumatism. Often an endocarditis may run its course ending in serious damage without subjective symptoms; physical signs, however, prove its presence in most cases early, hence the prognosis is improved in proportion to the early diagnosis and subsequent care given these patients. It must be remembered that, in rare cases, post-scarlatinal endocarditis may develop without subjective symptoms and may lead to permanently damaged valves. *Septic or malignant endocarditis* may complicate otitis, diphtheria or other mixed infections with scarletina and always ends fatally.

Irregularities of the heart, erratic behavior, at times surprisingly ***slow hearts*** alternating with *sudden acceleration,* are complications present during convalescence which are relieved by continued rest and abundant time.

Increasing systolic blood pressure with or without albuminuria during the first 2 or 3 weeks of scarlet fever, indicates obstruction in the renal circuit—hence nephritis. It is compensatory, and should be accepted as an evidence of Nature's effort to assist in the cure. When *dilatation* fol-

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lows this condition, *slight and insufficient hypertrophy, diffuse area of cardiac impulse,* the prognosis is less favorable.

Increased systolic blood pressure may be present during the early days of albuminuria, before there are other evidences of nephritis, and is likely to be the first suggestion of that complication.

The Kidneys.—*Acute nephritis* complicates one-seventh (1/7) of all cases of scarlet fever, and is a frequent cause of chronic kidney disease (interstitial and parenchymatous). Recovery is the rule in the majority of cases of scarlatinal nephritis, though it often leads to death. True scarlatinal nephritis is not likely to develop before the third week, and should not be confounded with the febrile albuminuria of the disease. It may begin to show itself as late as the 6th or 8th week. The greatest source of danger is *uremia.*

Uremic poisoning, usually arising suddenly, may be found with the mildest as well as the more severe nephritides. As a rule the complication may be expected if there have been the usual premonitory symptoms of uremic poisoning, including vomiting, headache, markedly reduced urinary secretions, slow pulse, with increased blood pressure. While uremia is a serious complication, *the prognosis is not entirely bad* and cases which appear serious, in which the coma and other evidences of surcharged blood are threatening, may fully recover. It is surprising to note how long children bear uremic poisoning in individual cases, and how completely they lift themselves out of it. *No case of uremia in a child is so severe that it may not recover.* I have seen children profoundly uremic with complete suppression of urine during 2, 3 and even 4 days, recover with return to normal kidney function and final restoration of normal kidney tissue, so far as I could tell from the subsequent histories of these cases. Pathologists and clinicians have repeatedly proved that two-thirds (2/3) or even more of our total kidney substance can be spared without serious inconvenience (Bradford). I have already referred to the association of heart and kidney lesions. *Nephritis* is a *frequent cause of cardiac asthenia,* leading to *severe dyspnea, cyanosis and edema of the lungs. Endo-* and *pericarditis* with nephritis are always serious. *Dropsies,* particularly *hydropericardium* and single or double *hydrothorax,* are complications due to nephritis, of grave significance. The prognosis in these cases should not be given as positively bad, for recovery does take place occasionally in spite of multiple complications. *The height of the fever* in *scarlatinal nephritis* when the symptoms are acute does not offer much of prognostic value. I have seen many cases in which the temperature for several days has continued high, which finally proved tractable and ran a short course.

In my practice I have found the quantity of *urine secreted* and the *heart condition* to offer *most reliable prognostic data.* Until the quantity of urine has increased and its color cleared, with reduction of casts and blood and a fair urea output, no positive prognosis can be given. Even

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in these cases we must leave a loop-hole in our prognosis for occasionally, for some reason, there is sudden suppression and a return of uremic symptoms. If with uremia or nephritis the heart fails to respond to treatment, if the pulse grows more tense and has periods of flabbiness and continues rapid, a guarded prognosis must be given.

Increasing anemia with *eye symptoms,* and *persistence of edema,* are evidences of extensive and obstinate kidney lesions, and influence prognosis accordingly, worse with cardiac instability.

Cases of nephritis which may be characterized as almost completely "*non-albuminuric*" in which a trace of albumin and few casts are found at long intervals, usually on arising in the morning (orthostatic albuminuria), yield to rest and treatment. When these remain unrecognized or untreated they are likely to be followed by chronic nephritis.

The duration of average nephritis with scarlet fever is from 2 to 4 weeks.

Arthritis.—*Non-suppurative polyarthritis* complicates scarlet fever in 6 per cent of cases. Developing during the second week usually or later as a rule it leads to recovery without damaged joints or endocardium. Occasionally endocarditis with positive physical signs develops, and almost all of these recover with but slight damage. In cases of scarlatinal arthritis rapid pulse and high temperature are not necessarily serious. In most cases both are high and yet recovery is the rule.

Adenitis.—Most cases of *suppurative adenitis* lead to full recovery. The types of diphtheritic and gangrenous adenitis complicating mixed infection (diphtheria, etc.), at the height of the disease, have been mentioned above and are always part of a serious process.

Adenitis with nephritis is a combination of serious moment though the larger number of these finally recover.

Résumé.—*Pneumonia* (*post-scarlatinal*) is often *associated with empyema* and offers a grave prognosis.

It may be accepted as a rule for the prognosis of scarlet fever that,

I. Added infection of any kind adds to the danger of the original disease.

II. No disease requires such a long period of observation of the kidney and the cardio-vascular system.

Finally, to classify systematically cases for prognosis, we accept Moser's division.

I. and II.—Favorable cases.
III. Doubtful cases.
IV. Hopeless cases.

Division I.—Includes cases without serious symptoms, reasonable temperature. Few or no pharyngeal symptoms, good general condition.

Division II.—Includes moderate intensity of symptoms. But one or

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two symptoms in the ascendancy. Moderate pharyngeal invasion. No suppurative otitis media. Moderate erythematous eruption. No heart weakness, no cyanosis. Fairly high temperature and pulse of good quality.

Divisions III. and IV.—Include the severe cases, grave, toxic and infectious forms (diphtheritic) above described, usually in children between the 1st and 4th year of life.

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III. Smallpox

(*Variola, Ger. Blattern, Fr. Petite vérole, It. Vaiuolo*)

Smallpox is an *eruptive disease* of *unknown origin, epidemic* or *endemic,* probably due to ultramicroscopic life, possibly of protozoic origin (Cytoryctes variolæ), and associated with *skin lesions, invasion of mucous membranes, and constitutional disturbances.*

Historical Data.—The disease was known long before the birth of Christ; it raged in China and India, and was brought to Egypt and the continent of Europe during the sixth century. Until the sixteenth century the disease remained in Southern Europe, when Germany was invaded. It is strange that during the thirteenth century serious epidemics decimated England without reaching Northern Europe. During the sixteenth century it was brought to America by the Spaniards. In 1718, Lady Mary Wortley Montague introduced inoculation into Europe, but it was associated with such painful results that it failed to gain a foothold. In 1798 the illustrious Jenner gave to the world the epoch-producing discovery of *vaccination* which robbed smallpox of its terror, and will with proper supervision, strict quarantine, and concerted action of the lay world and the medical profession as represented in the modern Science and Art of Preventive Medicine, ultimately efface it.

General Considerations.—*The character of the vaccination, it is now universally conceded, affects prognosis.* The *non- and insufficiently vaccinated* are likely to suffer from the *severer types of smallpox,* either discrete or confluent.

There seems in some families to be complete immunity to the disease, in some, repeated vaccinations remain negative. One colleague I have vaccinated seventeen times without reaction. He has been in the midst of malignant smallpox, treated many cases, but has never contracted the disease.

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One attack as a rule gives immunity, but there are so many exceptions, that the rule must be ignored if the public and the individual are to be protected. I have met several examples of mild first attacks of smallpox, in which second infections were severe and hemorrhagic. Reverse experiences I have also had.

Epidemics vary in virulence and are likely to present many features in which they differ. Some may be characterized as malignant, others benign. It is a rule that *the milder cases are found at the close of the epidemic.*

No *age* is exempt from the ravages of smallpox. It may attack the *fetus in utero*—usually with fatal result. Between the ages of one to forty the disease claims most of its victims. It is found in old age less frequently than during the active years of life. Prognosis of the disease in old age is bad. "The prognosis improves up to the age of ten, is more favorable until fifteen, and then gradually becomes less so, although the case mortality in discrete cases remains very small, at least until advanced old age" (White and Biernaski). The *sexes are equally attacked* and prognosis does not differ though *pregnancy and miscarriage, resulting from smallpox of the fetus and the mother, add to the number of serious cases in women.* It has been proved in all epidemics that *smallpox in pregnant women is likely to be malignant and strikingly fatal. Pregnancy invites the disease.*

The disease is prone to attack *negroes* and the mortality among these, in the unvaccinated, is larger than among the whites.

Stage of Incubation

The stage of incubation (10 to 13 days) offers no symptoms nor noteworthy data of use for prognostic purposes.

Stage of Invasion

The stage of invasion may be either mild or severe. The rule that an invasion with mild symptoms argues in favor of a benign smallpox, has so many exceptions that these must be kept in mind and should protect the clinician against a positive prognosis too early. There have been within my experience a number of cases in which the symptoms of this stage were unusually mild and reassuring, in which during the period of eruption I faced malignant disease of the pustulo-hemorrhagic and hemorrhagic types.

The *severe backache* (*rachialgia*) may be out of all proportion to the ultimate severity or benign nature of the disease.

Profound cerebral invasion is occasionally met in non-malignant cases. As a rule it is safe to consider somnolence, coma, delirium and marked subsultus indicative of the more severe form of the disease. *If these symptoms are present early in the period of invasion, and are associated with*

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high temperature in the adult or child, if the pulse is correspondingly disturbed, irregular and erratic, rapid and small, we may expect a severe course of the disease. Hurried respiration during the period of invasion, with rapid pulse, high temperature and delirium, argue against mild smallpox. *Marked enlargement of the spleen early is evidence of deep infection, and is of serious import* though *with "black smallpox" there is no enlargement as a rule. Albuminuria, during invasion with nephritis,* is always suggestive of great danger.

Rashes or prodromal exanthemata (invasion) may differ. In some cases these are *scarlatinal,* in others they resemble the *measle eruption* and are likely to be macular. They are evanescent in almost all cases (12 to 24 hours) and do not lead to desquamation. The deep scarlatinal eruptions are more significant prognostically than the moderate erythematous rash or the measle-like eruption. Macular eruptions as a rule are favorable; the *hemorrhagic prodromal eruption* is likely to remain, and is always of serious significance. *When both hemorrhagic and non-hemorrhagic macules* are present during this period, the prognosis must be guardedly given, for while this adds an element which may be interpreted as serious, a fair number of these cases recover.

Convincing symptoms of use for prognosis are found toward the end of the period of invasion and the established stage of eruption.

Stage of Eruption

In connection with the study of the prognosis of smallpox it will be wise at this juncture to present the accepted *classification* of its varieties made clear as a rule, only during the *stage of eruption.*

I. Variola vera.
   (a) Discrete smallpox.
   (b) Confluent smallpox.
II. Variola hemorrhagica (hemorrhagic smallpox).
   (a) Purpura variolosa (black smallpox).
   (b) Variola hemorrhagica pustulosa (pustular hemorrhagic smallpox).
III. Varioloid.
IV. Variola without eruption.

Pustulation.—Pustulation in the average case must be expected after vesiculation on the ninth day of the disease. A marked tendency early during pustulation to confluence is found in the more severe forms of the disease. *Pustulation, with limited eruption,* few lesions of the mucous membranes and but few constitutional symptoms, is always favorable. *Few pustules filled with blood*—this probably due to self-inflicted trauma—are not significant. With the pustulo-hemorrhagic type of the disease, a few

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bloody pustules do not influence the outcome. *Many pustules—hemorrhagic*—with *symptoms of pyemia*, are usually indications of severe infection and make the prognosis grave. *The earlier the hemorrhagic nature of the eruption in any form of the disease, the worse is the prognosis. Those cases justify a serious forecast in which there are hemorrhages into the skin early, and before pustulation or the pustulohemorrhagic condition is manifest.* These cases are unusually virulent. The prognosis is *grave if separate pustules, without known trauma fill with blood.*

The invasion of the *mucous membranes* (usually the mouth and throat, sometimes also the larynx, stomach, intestines, vulva, and rectum) is not as a rule of significance unless there are many pustules. If the invasion is far-reaching, the result is weakening and adds materially to the danger of the disease. *Large hemorrhages from mucous membranes are serious* and are usually associated with *variola hemorrhagica.*

Temperature.—A decided fall of *temperature* shortly after the appearance of the eruption, is always welcome and favorable. This is not at all unusual in cases which during the period of invasion, because of nervous symptoms, were considered serious. *In severe cases* there is but *little fall of temperature with the appearance of the eruption.* The temperature promptly rises to the height of the period of invasion and even higher; cerebral and other grave symptoms persist. It is safe to interpret a *decided drop* of temperature as vesiculation begins, *favorably, if it does not again mount to its former height.* In severe cases the drop of temperature even though appreciable, is of short duration; it is not likely however to be decided.

Persisting high temperature during pustulation is pyemic or streptococcic in its nature, and when associated with far-reaching confluence, is serious.

Blood.—During the stage of eruption the blood shows *marked leukocytosis* (12,000 to 24,000) with *lymphocytic increase.* This begins on the fourth to the sixth day of the disease and may continue during several weeks or months after full recovery. Neutrophilic leukocytes are only relatively diminished. Macgrath, Brinkerhoff and Bancroft found *in fatal cases and in those in which the skin lesions were severe and widespread, a decided lowering of the leukocytic count.* These observers also found increase of mononuclear lymphocytes.

General Statement.—The general statement is justified that small-pox (I. Variola Vera) may be either benign or malignant, that *the average mortality of all cases*—and *most of these are unvaccinated*—varies in different epidemics from 15 to 35 per cent.

I. *Variola vera*

(a) *Discrete Smallpox.*—Discrete smallpox has a mortality of 5 to 10 per cent.

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(b) *Confluent Smallpox.*—The mortality of *confluent smallpox* is high: *the greater the confluence, the worse the prognosis.* If confluence is not spread over the back, the prognosis is correspondingly better. If confluence is limited to the face and extremities the prognosis is worse than in the discrete form, but better than if over the trunk at the same time. Infants below two years of age all die when the eruption is confluent. Between two and five years of age one-fourth recover; after five years of age the mortality is lower; from ten to fourteen "the patient is more likely to recover than at any other age." "After fifteen years of age the percentage of deaths to recoveries increases steadily with advancing years" (MacCombie).

Laryngeal and pulmonary complications with *confluent smallpox,* cellulitis, and those unfavorable conditions mentioned under *General Considerations* add to the danger of confluence.

II. *Variola hemorrhagica* (*Hemorrhagic Smallpox*)

(a) *Purpura variolosa* (*Black Smallpox*).—Purpura variolosa is almost invariably fatal: recovery is so rare as to justify the gloomy forecast given. These patients die early in the disease, and as has already been mentioned, *without demonstrable enlargement of the spleen*—a fact of some prognostic value.

(b) *Variola hemorrhagica pustulosa* (*Pustular Hemorrhagic Smallpox*).—In the preceding pages mention has been made of a number of conditions which materially modify the prognosis of these cases. It is not as fatal as black smallpox (Purpura variolosa) but is more frequent. The disease if fully developed is grave; the majority of patients die, usually in collapse between the seventh and twelfth day of the disease.

III. *Varioloid*

This is a modified form of smallpox. The overwhelming proportion of patients if inoculated, were probably not properly vaccinated—hence not entirely protected—or have gone beyond the period of immunity. The duration of all the periods of the disease is materially reduced; many features of variola vera are absent; fever disappears with the modified eruption and rarely returns: when it does, it is of short duration and due to absorption of pus during pustulation.

Vesiculation and pustulation may not follow the formation of the papule; mucous membranes are usually untouched by the disease; *recovery is prompt, and as a rule without complication or sequel.*

IV. *Variola without Eruption*

This is always mild; it is usually found in well-protected subjects, or as the epidemic is fading. The symptoms of the stage of invasion sug-

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gest as a rule a mild form of the disease; occasionally there may be considerable constitutional disturbance, fever, rachalgia and anorexia. The appearance of the patient continues good, there may be a prodromal rash —usually macular, non-scarlatinal—*the disease ends favorably at the end of the period of invasion.*

Complications

These modify the prognosis as a rule during pustulation. Complications after the beginning of convalescence are infrequent.

Among the debilitating incidents are added *multiple phlegmons, deep abscesses of the muscles and suppurative adenitis.*

Erysipelas is always a serious complication, worse with the severer types of the disease: when facial and widespread with meningeal symptoms it usually leads to death.

Gangrene, local or widespread is serious.

Deep sepsis and *pyemia with confluence* are among the serious complications.

Bronchitis limited in extent is not unfavorable.

Invasion of the *smaller tubes* by *bronchial catarrh* (*bronchiolitis*) adds a large element of danger in the possible development of *bronchopneumonia,* which is not unusual.

Croupous pneumonia is not frequent, occasionally when present, it is followed by *lung abscess.*

Purulent thrombosis is always a serious complication.

Pleurisy and *empyema* occasionally follow; as a rule the latter is the more serious, but if a late manifestation and relieved by drainage, most patients recover. Occasionally *pulmonary tuberculosis* has been a sequal of smallpox. Rolly makes the statement that all lung and pleural complications give a bad prognosis.

Invasion of the *mucous membranes* has been mentioned in the preceding pages, also edema of the glottis—a threatening complication.

The complications due to *eye, ear* and *nose* invasion demand the consideration of workers in special fields. They are often destructive and permanent. *Eye complications* are present in from six to ten per cent of all cases. Blindness due to suppurative disease of the eye, opacities of the cornea, and other deforming and damaging conditions depend on eruptive lesions, sepsis or pyemia.

Brain complications have been mentioned as occurring during the acute stages of the disease and their prognostic significance discussed. There are cases in which *acute encephalitis, aphasia* consecutive to softening of brain substance, have proved fatal. Leyden has reported cases complicated with *diffuse myelitis, insular sclerosis* and *acute ascending paralysis* (Quoted by Rolly). In the epidemics of Central New York,

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peripheral neuritis was exceedingly rare and psychic disturbances mentioned by many observers have been absent.

Suppurative arthritis is a serious and damaging complication: when these patients recover, anchyloses are the rule.

The *degenerative changes* lead in serious cases to *myocardial weakness, kidney invasion,* while *septic endocarditis* is associated with a limited number of cases and invariably leads to death. *Pericarditis,* occasionally purulent, has proved fatal.

Vaccination—Vaccinia

But little space need be given to the prognosis of vaccination itself; when done under strict antiseptic precautions, and these are continued, or if after a septic vaccination such strict cleanliness of the wound and person as the intelligent physician directs is practiced, there is practically no danger of infection if a pure animal lymph is used. The following conclusions are justified by large clinical experience and will prevent complications and annoyance if heeded, and the prognosis of vaccination will be uniformly good.

Conclusions:—1. *Arm to arm inoculation* is justified.

2. *Human scabs or crusts* are never to be used.

3. *Vaccination* with *animal lymph* from reliable sources, *preferably under State control,* offers the best prognosis.

4. Attention to detail and *strict asepsis are demanded;* the subject and the operator need to be equally clean.

5. A *sick child* should not be vaccinated unless in the midst of an epidemic, or immediately after exposure to the disease.

6. Children or adults showing *acute syphilitic lesions* will *react unfavorably and should first be subjected to antispecific treatment and later vaccinated,* unless there is danger of immediate smallpox infection.

7. The same advice should be accepted in connection with *congenital syphilitics.*

8. Children or adults, reduced in health, with *active tuberculosis, strikingly anemic, cachectic, with suppurating glands* or those suffering from *acute disease of the nervous system,* including *chorea,* should first be prepared and later vaccinated.

9. *Tetanus* will not follow vaccination unless there has been contamination either through the lymph, from the body of the vaccinated subject or through dressings, or as the result of faulty technic (instruments, skin, etc.).

10. *Auto-infection* is avoidable, and is evidence of carelessness on the part of the vaccinated or those responsible for his care.

11. *Disease, i. e., syphilis, acute infection, tuberculosis, "scrophula," and smallpox itself,* is never spread by clean vaccination.

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12. *The vaccination of children* has no influence in preparing ready culture media in the body for the development of the other acute exanthemata (measles, scarlet fever, etc.).

Considerations and Statistics.—*How the prognosis of smallpox has been influenced by vaccination* requires no detailed consideration: even the intelligent layman has this knowledge at his tongue's end. A few telling statistics may be added to round this chapter. There was a time when *smallpox was the direct cause of 1/7 of all deaths,* and this, in the *civilized countries of the earth*—as fatal as was tuberculosis during the last quarter of the 19th century. *During the 18th century* 30,000 *victims* were annually claimed *in France;* in 1796, 25,646 *died in Prussia* when its population was 7,000,000. *In Berlin 1/12 of all deaths were due to smallpox during* the last decade of the 18th century.

In countries today where vaccination is obligatory, note the change. *Smallpox has been reduced, among the properly vaccinated* to 0.25 to 0.35 per 100,000 population. The detailed statistics of Prussia show the disease to be present among 0.25 per 100,000 of population. In England and Wales during 1910 there were but 19 deaths due to smallpox. In the United States during 1909 and 1910 there were 54,451 cases of smallpox with 565 deaths—about 1 per cent mortality among the infected.

Proper regulation of vaccination, making it *obligatory in all countries,* in all of our own states, well guarded *quarantine* after the early *recognition* of the disease, *revaccination* at regular intervals (six to ten years) will surely lead to the disappearance of the disease.

Finally we would call attention to the fact that protection conferred by vaccination is in direct proportion to the thoroughness of the operation and the number of cicatrices. Marson (London Smallpox Hospital) brought the results of his observations to the notice of the Royal Commission of England through Sir Richard Thorne, from which I take the following data:

Cases of Smallpox Classified According to the Vaccination Marks Borne by Each Patient Respectively.	Percentage of Deaths in Each Class Respectively Uncorrected.*		Percentage of Deaths in Each Class Respectively Corrected.*	
	1836–51	1852–67	1836–51	1852–67
1. Stated to have been vaccinated, but having no cicatrix	25.5	40.3	21.7	39.4
2. Having one vaccine cicatrix	9.2	14.8	7.6	13.8
3. Having two vaccine cicatrices	6.0	8.7	4.3	7.7
4. Having three vaccine cicatrices	3.6	3.7	1.8	3.0
5. Having four or more vaccine cicatrices.	1.1	1.9	0.7	0.9
Unvaccinated	37.5	35.7	35.5	34.9

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Vaccination Scars.	Total Cases.	Confluent and Hemorrhagic.	Deaths.
One.....	886	177 or 20. per cent.	101 or 11.4 per cent.
Two.....	589	83 or 14.1 per cent.	44 or 7.3 per cent.
Three.....	94	13 or 13.8 per cent.	4 or 4.2 per cent.
Four.....	74	9 or 12.2 per cent.	2 or 2.8 per cent.

* The terms uncorrected and corrected are used to signify the inclusion or exclusion of those fatal cases of smallpox in which the patient suffered from some other disease superadded to the smallpox.

References

Macgrath, Brinkerhoff & Bancroft. *J. of Med. Research, 1904.*

MacCombie. *Allbutt & Rolleston, System of Medicine. 2. ed., 529.*

Rolly. *Mohr & Staehelin, Handbuch der Inneren Medizin. 1911, i, 169.*

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White & Biernaski. *Bain, Text Book of Medicine.*

IV. Varicella

(Windpocken, Gr. Spitzpocken, Chicken pox, Varicelle, Fr. Petit verole volante)

Chicken pox is a highly contagious disease of childhood (adults are rarely attacked) of unknown origin; it is characterized by a vesicular skin eruption, which finally becomes pustular; is associated with mild constitutional symptoms, promptly yields and ends in full recovery, with developed immunity (99 per cent of cases) to the disease.

The prognosis of varicella is almost uniformly good. In an experience of thirty-five years I number but one death due to the disease, that of a feeble child, four months of age, who died in convulsions with the characteristic rash fully developed. *Deaths atttributed to varicella,* have, in all probability in the majority of cases been *unrecognized smallpox,* unless in correctly diagnosticated cases there have been serious *complications—which are exceedingly rare.*

Rolly reports the autopsy of a child who died on the thirty-sixth day of the disease after a long period of dysentery following chicken pox, in which one of the pustules became gangrenous. There was also albuminuria with hyaline casts. The autopsy showed dysenteric lesions in the large intestines, enlarged mesenteric glands, and cloudy degeneration of the cortical substance of the kidney. In this case dysentery was probably an accidental accompaniment of varicella.

Occasionally a *death* has been reported during *chicken pox epidemics*

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due to *hemorrhagic accompaniments.* In most of these cases the children were either sick or reduced by previous illness.

Complications

Nephritis is a rare complication, usually ending in recovery. This is likely to be of *hemorrhagic* nature.

Chorea has followed close upon convalescence, in children predisposed. *Hemiplegia, encephalitis, pericarditis, pleurisy, suppurating adenitis, mediastinal abscess* are also among the rare sequelæ.

Poly- or *monarthritis,* usually mild, have been present in a very small per cent of cases. *Recovery without endocardial disturbance is the rule.* Rolly makes the following statement: "Chicken pox influences tuberculous disease, as does measles, unfavorably. Tuberculosis is positively lighted into activity to such a degree that the patients usually die within a short time." The *combination* of *chicken pox* with other acute exanthemata, *scarlatina and measles,* is an occasional coincidence. *The prognosis depends entirely in these cases upon the severity of the infection other than varicella,* which is not materially influenced by the presence of the latter disease.

Reference

Rolly. *Mohr & Staehelin, Handbuch der Inneren Medizin, i., 142.*

V. Measles

(*Morbilli, Rougeole, Rosolia*)

Measles is an acute exanthematous, directly contagious disease of early childhood (1st to 5th year); it is epidemic, characterized by fever, catarrhal inflammation of the air passages and photophobia, a disease in which positive immunity is not produced by one or more attacks, though as a rule the disease is not repeated. The bacterial cause of the disease is unknown. Its *period of incubation* is from seven to fourteen days.

Patients continue to carry the contagion during at least sixteen days, *the length of the period of safe quarantine. The blood and secretions,* the desquamated skin, the clothing and bedding, hold the contagious element and *transfer the disease to the healthy,* in all probability, *by direct contact.*

The disease is contagious during the period of invasion (3 to 4 days before the eruption) and after, during from ten to sixteen days. *The severity of subsequent attacks is not influenced by previous infection.*

The *prognosis of uncomplicated measles* is almost uniformly good.

The disease is either *mild* or *malignant. Malignant measles* is rare and is of *hemorrhagic character,* associated with deep discoloration of the eruption, marked invasion of the nervous system, degenerative changes in

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the heart and kidneys, and causes death in most cases between the second and fifth day of the eruption. In some malignant cases the period of invasion is characterized by severe symptoms. There may be *hemorrhages from mucous surfaces* (epistaxis, etc.), a *purpuric eruption*, and children may die before the true measle rash appears. Fortunately, as already stated, these cases are exceedingly rare.

The number of *Koplik spots* bears no relation to the severity of the disease.

Temperature.—In the majority of favorable cases the *temperature* averages between 102°-104° F., with corresponding acceleration of the heart action. The more severe cases are characterized by the deeper, "darker," papular eruptions. The *papules* of *mild* measles disappear as a rule on deep pressure, the *hemorrhagic papules* do not disappear.

Conjunctivitis.—The severity of the *conjunctivitis* in the majority of cases bears no relation to the severity of the disease. It not infrequently happens that measles with mild constitutional symptoms may have severe catarrhal conjunctivitis, as well as harassing bronchitis.

Blood.—*Leukopenia* is the rule in measles; there is in favorable cases disappearance of *lymphocytes* (usually in the ascendency during early childhood) and relative increase of *neutrophilic leukocytes.* The white count in the average case is between 2,800 and 3,400. *Leukocytosis during the period of eruption* indicates the presence of a complication. *Lymphatic* (cervical, mainly) *enlargements* are the rule are not of serious moment, and recede during the period of convalescence.

Urine.—*Febrile albuminuria* is frequent and is found with marked constitutional involvement; it is not of serious importance save in the hemorrhagic types of the disease.

The *mildest cases* are those without catarrhal symptoms or few only, a modified rash, and but slight febrile movement.

The severe types (*non-malignant*) of the disease in which the prognosis may be doubtful are those in which with a deep colored eruption there is hyperpyrexia, brain symptoms including the typhoid conditions, delirium, involuntary discharge of urine and frequent diarrheal stools, with rapid small dicrotic pulse. The periods of incubation *and invasion* may be associated with the symptoms of severe infection, which in occasional cases cease with the appearance of the eruption—the entire picture of the disease changing for the better suddenly, with fall of temperature and improved pulse. *The reverse may also happen,* i. e., mild periods of incubation and invasion with increase in the severity of the symptoms during the period of eruption.

The Skin.—*Cyanosis* of the skin, a blue appearance of the papules, is found in the graver forms of the disease. The heart in these cases offers the best indications for prognosis; with evidences of cyanosis its musculature is usually weakened by toxins, previous or associated disease.

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Mortality.—The rule may be accepted that *measles without complications* offers an exceptionally favorable prognosis. The *average mortality* of all cases of measles, with and without complications, is between four and 6 per cent, varying with different epidemics. The mortality is highest during the first three years of life and lowest between the fourth and twentieth year. Measles after the forty-fifth to fiftieth year is less favorable than during the more active years of life.

Complications

Bronchopneumonia is the gravest of all of the complications of measles; one-half to three-quarters of all deaths following measle infection are due to it.

Bronchitis invading the smaller tubes is always a menace and when in these cases there is sudden increase of respiration with rising temperature and active playing of the accessory muscles of respiration, the development of secondary bronchopneumonia may be expected, and the prognosis is correspondingly serious. In some of these cases *atelectasis* may follow *bronchiolitis*—always a serious complication—or it may accompany or follow bronchopneumonia.

Bronchopneumonia is a complication of measles in epidemics of average severity and duration in from five to eight per cent of all cases. The *mortality of bronchopneumonia* varies in different epidemics and ranges between 40 to 70 per cent.

Measle infection invites the development of *pulmonary tuberculosis* and lights *latent tuberculous diseases* into activity. Besides this, the *glandular system* is so changed by the infection that it offers a suitable habitat for the tubercle bacillus *from which long periods after infection, tuberculosis may spread.* This is particularly true of the *bronchial nodes* in measles as well as whooping cough and other non-tuberculous infections of the upper respiratory organs. In some cases the tuberculosis resulting runs an acute and rapid course.

Laryngitis may at times be severe, considerable edema may be present, and at times, ulceration; recovery is the rule. *Croup* with modern treatment offers a favorable prognosis.

Whooping cough accompanying measles always increases the dangers of complications; bronchopneumonia is always to be feared and likely to be fatal with this combination.

Ulcerative stomatitis or the usual less severe forms add painful symptoms, but without further complication recovery follows slowly.

Cancrum oris (*Noma*) is always serious, it may lead to large loss of tissue and has in my experience proved fatal in three-fourths of all cases.

Otitis media suppurativa is present in about 7 per cent of all cases of measles, usually during convalescence. But few cases receiving prompt

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attention lead to serious complications, such as *mastoiditis, sinus thrombosis or consecutive meningitis.*

Non-tuberculous adenitis, enlarged lymphatic glands following measles —usually in the cervical region—are likely to be associated with adenoids, and under surgical treatment and improved hygienic surroundings yield promptly.

Persistent enlargement of cervical glands after measles even without fever or evidences of *cheesy degeneration* should be considered to be of tuberculous origin. Prognosis and treatment should be accordingly framed.

Diarrhea and other symptoms of *gastroenteritis* early or late, may weaken the child but offer a favorable prognosis in the absence of other complications.

Jaundice has never complicated my cases. It has been reported by others (Friedjung), with favorable outcome.

Heart complications are rare. The malignant cases promptly show *vasomotor paralysis,* the governing spinal centers are soon fatigued by the toxins, and there are also degenerative changes in the myocardium itself.

Nephritis is rare; it is not as serious as with scarlet fever and only rarely does it lead to death. If present it runs a benign course and leads to recovery and full restoration of kidney tissue in from three weeks to two months.

Permanent damage to the eye resulting from *catarrhal conjunctivitis* is unusual. Occasionally with *keratitis* slight opacities have remained.

Brain complications are usually secondary when late. *Early convulsions* in young children are not always of serious import. *Early delirium and the typhoid condition* are present in the severer infections and with complicating meningitis and bronchopneumonia. They may also follow or accompany otitis, mastoid invasion and nephritis.

Tuberculous meningitis may promptly follow measles; in the majority of these cases latent deposits were stimulated to activity by the added infection. Rarely is measles followed by *polyarthritis* with or without mild endocarditis; the same is true of *pleurisy.* The prognosis of these complications is good.

Rolly contends that when *scarlet fever* complicates measles, the prognosis is usually good; when however measles is added to existing scarlet fever, the course of the measle infection is severe and long and the mortality is higher.

The association of *measles* and *whooping cough* has already been mentioned in connection with bronchopneumonia as a serious complication.

Diphtheria (positive presence of the diphtheria bacillus in the diseased tonsils, etc.) when coincident with measles, is likely to prove serious and justifies a guarded forecast; when measles follows after diphtheria has run its course, the prognosis is decidedly better—usually full recovery results.

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References

Friedjung. *Allgem. Wien. med. Ztschr.,* ***1910.***

Rolly. *Mohr & Staehelin, Handbuch der Inneren Medizin.* ***1911, i.***

VI. German Measles

(*Rötheln, Epidemic Roseola, Rubeola, Roseole epidemique*)

German measles is an acute contagious disease of uncertain origin, epidemic or endemic; in its typical development it includes a rash, inflammation of the cervical lymphatics, and moderate elevation of temperature. It is less contagious than measles, and is probably transmitted by fomites.

Second attacks are frequent.

Children between the *ages* of *two and ten are usually attacked.*

The period of incubation is unusually long—fourteen to twenty days.

The disease is so mild in its manifestations that the physician's usual function is to satisfy the parent by his differential diagnosis and the assurance of prompt recovery of the patient in from four to eight days. Cases with severe symptoms are exceedingly rare.

Occasionally an epidemic includes cases in which separate symptoms are severe, as general lymphatic enlargement and slight nervous manifestations, with possible convulsions in the younger children, but these too make satisfactory recoveries.

Recrudescence and *relapses* are occasional experiences.

Complications

Complications are infrequent. In our experience we have rarely been called to attend a child for any sequel of German measles.

Among the complications mentioned by others are, *bronchitis,* which always yields to treatment promptly; *bronchopneumonia,* which, rarely present, is less dangerous than with other exanthemata, as measles; *acute gastroenteritis* of transitory duration; and mild, slight *enlargement of the thyroid gland* with tenderness; and in some cases persistence during several months of enlarged lymphatics.

Koplik has reported *abortive cases* without marked enlargement of lymphatics, no eruption, slight febrile movement leading to prompt recovery.

Reference

Koplik. *Arch. f. Kinderkrankh.,* ***1900.***

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VII. Yellow Fever

(*Black Vomit, Fr. Fièvre jaune, Span. Fiebre amarilla, Span. Vomito negro or prieto, Ital. Febbre gialla, Ger. Gelbes Fieber, Lat. Typhus icteroides*)

Yellow fever is an acute pestilential infectious disease, epidemic, of uncertain origin, conveyed by the mosquito, Stegomyia fasciata (calopus), which in the past has raged in tropical and insular America between the 45° north and 35° south latitude. The disease is characterized by a fever continuing for two or three days, followed by a marked remission which may end either in convalescence or the patient may pass into a critical stage in which there is "black vomit," jaundice, hemorrhages, albuminuria, possible suppression of urine, and a typhoid condition with mental and nervous symptoms.

The disease is always dependent on a temperature not lower than 70° F., hence *the epidemic ends with the first frost.*

The disease was brought to San Domingo and Porto Rico by Columbus in 1493 in all probability. It rages along river and ocean fronts and is not likely to make much headway in country districts. *Crowded cities,* especially the neglected parts near the water, suffer most during epidemics. *Filth, marsh, faulty sanitary conditions* invite the mosquito and spread the disease.

Any American writing on the prophylaxis and prognosis of yellow fever must be stimulated by the achievements of American medicine. What the unselfish and practically unrewarded sacrifices of Walter Reed, Carroll, Lazear, Agramonte in the Western Hemisphere, and Myers of the Liverpool Commission, which resulted in the control of the disease in tropical and insular America, with the practical application by Colonel Gorgas of the facts thus furnished have accomplished for mankind, cannot be fully estimated today. The "Augean stables" have been cleansed, cities have been made safe, commerce, formerly stagnant during epidemics and long after, has been extended without obstacle, and the Panama Canal, the greatest achievement of modern times, has been completed, connecting the Atlantic and Pacific oceans, at the same time transforming a zone formerly pestridden into an inviting and healthy country.

There has been no serious epidemic in the United States since 1897 when the disease last raged in New Orleans with a much lower death rate than during former epidemics. In all probability the disease will be completely effaced and the writing of the chapter on its prognosis will consequently prove to be a work of supererogation.

Special Considerations.—There are a few points bearing on the prognosis which should be considered. The degree of the *fever of the period of invasion* is usually in direct proportion to the severity of the disease.

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The more rapid the *pulse* the more serious is the infection.

Early *black vomitus* or *hemorrhage* is always serious.

The *collapse* following the fall of temperature may promptly end life, for *in no other disease does the heart muscle degenerate so rapidly as in yellow fever.* Fatty granules displace the normal muscle; the heart cavities are filled with dark brownish black blood.

With the *end of the remission* in the serious cases symptoms referable to various internal organs present. *Deep jaundice* with *hemorrhagic tendencies, profuse black vomit* and *albuminuria with casts*, or complete *suppression of urine* make the prognosis bad, and with these symptoms from 50 to 60 per cent of patients have died.

Disappearance of albumin and casts, and return of urinary function are favorable indications.

Cases without deep jaundice, hemorrhages and with but slight albuminuria, few casts, moderate vomiting after remission offer a favorable prognosis.

Large bloody stools are often found with profuse black vomit and are an expression of hemorrhage, and are serious.

Free perspiration during the first stage is always favorable.

An *algid state* of the patient at any time, with collapse, with or without hemorrhages, is among the most dangerous conditions presented by the yellow fever patient.

Hemorrhage is a cause of death in a proportion of cases.

Ecchymotic spots with *multiple symptoms* are unfavorable.

Hemoglobin is reduced. *White blood corpuscles* vary between 5,000 and 20,000. *Polynuclears* are increased; *eosinophilia* is rare. *Hemoglobinemia* and *hypoleukocytosis* are to be expected in the average cases.

Marked degenerative changes in the *liver* are present and accompany the serious cases, with deep jaundice, great *collapse* and associated *nephritis.* In spite of great weakness following the first stage of the disease, those patients are likely to recover who do not have a return of fever, whose skin does not become dusky, and who are without typhoid symptoms.

Rapid pulse in the *second stage of the disease* with *typhoid or brain symptoms*, including *stupor, sordes* accumulating on the teeth, *dark and dry foul tongue*, increasing *jaundice*, occasional *convulsions, and suppression of urine* are unfavorable.

If the patient enters the *third stage*, and the temperature shows a decided rise and many of the untoward symptoms mentioned in the preceding paragraph are present, death is likely to follow.

The period from the fifth to the seventh days is most ominous.

No case of yellow fever is safe until convalescence has been fully established.

The *negro* is less susceptible to yellow fever than is the white man, and when infected bears the disease better. There is a difference of 30

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per cent in the mortality in some epidemics between the death rate of whites and blacks.

The *Chinese* are more resistant than whites.

The *American Indian* is but little less liable to the disease than is the European (Davidson).

The larger number of victims are claimed between the twentieth and fortieth years of life. Yellow fever is more fatal to men than to women; children bear the disease better than do adults.

Immunity follows a single attack of the disease: exceptions to this are rare. The *mortality* varies in different epidemics from 15 to 85 per cent and is highest among alcoholics; lower in precincts where hygienic conditions are good.

Reference

Davidson. *Allbutt & Rolleston, System of Medicine. ii., part ii.*

VIII. Foot and Mouth Disease

The disease rarely occurs in man. It is characterized by the formation of *vesicles, blebs and bullæ in the mouth, nose, lips, on the tongue* (often with *salivation*), and on the *fingers* and *toes.* The *bacteriologic cause* of the disease *is unknown. The disease is contracted from cattle—goats, sheep and pigs.* The *udder* and *mammary glands* of cattle are often diseased and from these sources the disease may be spread.

The contagion may be conveyed through milk, butter, cheese, sputum, nasal secretions; particularly by the rich cream of the infected animals. *Boiling the milk destroys the disease-producing power, simple heating does not. Direct contact* with the infected does not cause the disease save in the rarest instances: the skin of workers in dairies is seldom infected. The most frequent cause is the drinking of raw milk, rich cream and milk products (cheese, etc.).

The *formation of vesicles* is associated with more or less *febrile movement* in man. The *buccal mucosa* is the most frequent seat of the *vesicular eruption* after a period of incubation varying from two to ten days. Fever with malaise, and often other evidences of constitutional disturbances, are present from the beginning. Dryness and burning sensation in the mouth are among the disagreeable symptoms. The vesicles appear on the third to sixth days of the disease with a fall of temperature and *salivation.* The symptoms in the adult need cause no alarm in spite of an added *diarrhea* in some cases. *In very young children,* nurslings particularly, who are infected, *depleting diarrhea* may occasionally cause death and the prognosis is less favorable than in the adult. Symptoms are likely to persist during two weeks in mild cases, as long as four to eight weeks in the severer infections, with considerable loss of flesh and strength. The healing process is complete, the ulcers left by the vesicles

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are promptly covered with epithelium and the neighboring inflammation subsides.

The *lesions* about the *fingers* and *toes* are characteristic. Vesicles or bullæ form, leading to limited superficial losses of tissue, often pus deposits about the nails (*paronychia*)—all of which heal in from two to eight weeks.

The average duration of the disease is fourteen days. In occasional large epidemics the mortality has reached eight per cent.

When there are doubts concerning the diagnosis, consequently prognosis as well, these may be overcome by the *inoculation* of sheep or goat with the serum or pus of the vesicle.

Prophylactic measures will ultimately lead to the extermination of the disease, for it is easy to recognize the presence of the epizoötic in a dairy and to institute prompt quarantine against the infected cattle and the milk.

IX. Ephemeral Fever

(*Febricula, Symptomatic Fever*)

Ephemeral fever is a febril condition of short duration and of unknown origin, which in all probability is *symptomatic* and hardly deserves to be dignified as a disease *per se*.

It has always seemed to me that whenever the clinician has been forced to diagnosticate "Ephemeral fever" he admits *ignorance of the cause of the febrile disturbance. Symptomatic fever* would in all probability better characterize the complex than "ephemeral fever."

Ephemeral fever may be an *expression of one of several infections*, and is in some cases an *abortive form* of *typhoid, paratyphoid, scarlet fever, measles, rheumatism* (arthritis) or even *pneumonia*. This conclusion is justified because the disease is found at times of *epidemics* of the above mentioned diseases. *Sporadic cases* are frequent.

In *children* the complex is often *coincident with digestive disturbances* due to dietetic errors. It has, in *children susceptible to febrile movement* on slight cause, repeated itself at short intervals during a number of years, usually ending, never to return after the seventh to tenth year of life. The *duration* is rarely longer than three days: usually from twenty-four to thirty-six hours. I know of no fatal cases of the disease.

X. Infectious Jaundice—Weil's Disease (1886)

(*Epidemic Catarrhal Jaundice, Morbus Weilii*)

Weil's Disease is an *epidemic* acute infection, characterized by *gastric symptoms*, fever, *jaundice, constitutional symptoms, albuminuria*, and

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severe *muscular pains.* There is in severe cases *delirium, nephritis, hematemesis, melena* and *epistaxis.* The *pulse* is rapid in proportion to the severity of the infection.

In the average cases the *temperature* may be continuously high during from six to seven days. In some of these there may be *delirium* which is not of serious import.

As a rule, the *evidences of constitutional infection* begin to improve with the end of the first or the beginning of the second week.

Prostration may appear alarming during several days but if the pulse remains of fair character, the disease being self limited, patients bear the symptoms through the critical period and recover. The disease appears among consumers of *meat* mainly, and has been found in *butchers* very largely.

As patients recover, the *spleen* and *liver* recede and with the disappearance of *jaundice* and *albuminuria,* normal functions are restored. The disease shows a low *mortality,* though in some endemics it has reached 10 per cent.

Relapse after the end of seven to ten days complicates one-half of all cases; in some, the fever then continues during three to four weeks; most of these recover. *Convalescence* is slow. In *fatal cases* there is an increase of *kidney symptoms,* and deep invasion of the *nervous system; purpuric* spots cover the body and there are *hemorrhages from the mucous membranes.* Marked *heart weakness* with *myocarditis* may end the scene. In some cases *pneumonic infection* may prove a serious complication.

XI. Sweating Sickness

(*Febris miliaris*)

Sweating sickness is characterized by fever, *excessive sweating,* and an *eruption of miliary vesicles.* It has never been epidemic in the United States so far as I can determine by a search of medical literature. The disease proved fatal at the end of the fifteenth century in a large number of cases during the first epidemic of which there is a record in England, and has been known since in Germany and on the continent as the "English sweat." Hirsch in his monumental work reports 194 epidemics between 1718-1879. Epidemics begin and end suddenly, and never continue long. Large numbers are stricken during epidemics; the *active* and *healthy adult* and *women* are most subject to the disease.

The *duration* of the disease averages seven days.

The disease during the initial English epidemic had a high *mortality,* 80 to 90 per cent; in recent epidemics, on the Continent, the death rate has been 20 per cent. Death took place on the third or fourth day usually.

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The *prognosis* is worse early in the epidemic than after it has spent its force and is ending.

In some cases *death has been sudden* during the first or second day of infection.

Reference

Hirsch. *Handbuch der Histor.-Geograph. Pathologie. 2. ed., 1881.*

XII. Herpetic Fever

(*Febris herpetica*)

Herpetic fever is a symptom complex of unknown origin, characterized by *fever*—usually mild—with some *constitutional disturbances*, in rare cases severe, slight *enlargement of the spleen.* All of these symptoms continue during two to five days when the *herpetiform vesicular eruption* appears, usually covering a considerable portion of the body, though at times only a cheek and adjacent skin or an ear or the neck; occasionally the eruption may become *hemorrhagic.* In rare cases in which there is an *hemorrhagic* tendency, *nephritis hemorrhagica develops.* The *prognosis* is good; *recovery* is the rule; the *duration* is short. *Relapse* often occurs and is of short duration, lasting about one day.

XIII. The Fourth Disease

(*Dukes' Disease, Filaton-Dukes' Disease, Rubeola scarlatinosa, Scarlatinoid*)

This is an acute symptom complex which the Americans and Germans have not yet entirely accepted as a disease *per se*, fully described by Dukes, bearing close resemblance to abortive scarlet fever and also rötheln, with less desquamation than follows the former but greater than in the latter.

The *constitutional disturbances* are of short duration; the *period of transmission* of infection is also short, while the *period of incubation* is unusually long (9 to 20, or even 30 days).

The prognosis is uniformly good and there are no complications or sequelae.

XIV. Epidemic Parotitis

(*Mumps*)

Mumps is an acute epidemic disease, characterized by swelling and non-suppurative inflammation of both parotid glands, *contagious*, of uncertain origin, associated with moderate constitutional disturbance, a long period of incubation (eighteen days) leading to full recovery in from seven to ten days. *Immunity* follows a single attack with rare exceptions.

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Complications.—In about 25 to 30 per cent of male adults, rarely in young boys, the infection is associated with *orchitis*, usually single, and attacks the *right testicle oftener* than the left. The complication runs its course in from seven to fourteen days causing some *atrophy of the testicle* in from 30 to 40 per cent of cases. In rare cases the changed testicle in after years has been found *tuberculous*. There is but insignificant enlargement of the spleen. In exceptional cases, a *chronic swelling of the parotid gland* follows which persists during many years.

Among the serious complications reported in medical literature which have resulted in death, are *meningitis, encephalitis, gangrene of the parotid, nephritis and laryngitis* (*croup*). Less serious complications have included *otitis media and externa, Meniere's disease*, and insignificant ocular disturbances, such as *conjunctivitis, keratitis and iritis*—rarely *paralysis of the ocular nerves. Nephritis* is rare; slight *albuminuria* with few hyaline casts is present in occasional cases.

Symptoms referable to the *nervous system* if serious are an expression usually of added infection. There may, in rare cases, be a *transitory typhoid condition* from which the patients promptly lift themselves: this is an early complex.

Serious *heart lesions*, endo- and pericarditis I have not met in my epidemics though others have reported these at long intervals. *Polyarthritis* when present is of short duration, benign and without endocarditis.

Severe joint and muscle pains (myalgia) are frequent. I have never met a case of *oöphoritis* due to epidemic parotitis. Many hold that there is a *reciprocal relation which invites change in the ovaries when the parotid is diseased, and vice versa.*

Mortality.—The low *mortality* of epidemic mumps is shown by the statistics of Ringberg who found seven deaths in 58,331 cases of the disease.

Reference

Ringberg. Quoted by Krause. Mohr & Staehelin, Handbuch der inneren Medizin. 1911. i, 239.

XV. Glandular Fever—Pfeiffer's Disease

(*Drüsenfieber*)

Pfeiffer's disease or *glandular fever* is an acute febrile disease of childhood—it also occasionally attacks adults—of uncertain origin, characterized by headache, dysphagia, congested tonsils and pharynx, by enlargement of the *cervical lymphatics* (usually bilateral) with tenderness; in some cases many distant glands are involved (*axillary, inguinal, mesenteric*, et cetera). The *febrile period* ends in from three to seven days; the *glandular enlargement* and *pharyngeal redness* may appear any time between the second and fifth day.

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In a recent *epidemic* in Dryden, New York, there were as a rule, *bilateral enlargements* of the *cervical lymphatics* which appeared *without redness* of the skin. The children were without marked constitutional disturbances after the fourth day; the glandular enlargements gradually melted away in from seven to twenty-one days.

In the counties between Central and Eastern New York *sporadic* cases have occasionally followed very limited endemics. As a rule in these districts the disease has not attacked many children.

The *duration* of the disease is short. The *fever* ends before the seventh or eighth day. Recovery has been complete in all cases seen, and without complication. No case of which I have knowledge has ended in suppuration, though such cases have been reported by others; neither has *nephritis, otitis* nor *retropharyngeal abscess* followed.

Suppuration has seemed to be more frequent in the adult than in children.

The associated *edema* of the soft palate and palatine folds may prove exceedingly painful and extension to the glottis serious.

In the *anemic*, and children otherwise *reduced in health*, convalescence has been somewhat protracted.

XVI. Hydrophobia

(*Rabies, Lyssa, Wutkrankheit*)

Hydrophobia is a disease the bacterial origin of which is unknown, transmitted to man by the bite of rabid animals through the infected saliva, especially that of the dog. The deeper the bite the greater the laceration and the more saliva introduced, the more likely is hydrophobia to follow.

The majority bitten by rabid dogs never develop rabies. The figures given by Romberg, showing 15 to 20 per cent of those bitten to be infected, correspond very closely with those of American and other continental observers.

Hydrophobia follows bites of the exposed parts of the body—hands and face oftener than bites where clothing has served to protect and hold the saliva of the rabid animal. The development of the disease depends in all probability upon the injury and infection of the peripheral nerves which serve to transmit the infection to the central nervous system, i. e., the cord and the medulla.

An important prognostic fact is the possibility of the transmission of the disease from the infected animal to man several days before the onset of symptoms in the former.

The period of incubation is unusually long, varying from one to nine weeks—occasionally several months.

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Those bitten by rabid dogs who have not received the Pasteur treatment, in spite of a negative condition are not to be considered immune until the end of at least three months.

The healing of the wound inflicted by a rabid animal, in one unprotected by inoculation (Pasteur), does not in any way argue against or in favor of ultimate infection.

Burning, itching, throbbing and pain, when not due to autosuggestion, are soon followed by swelling, depression, melancholia, malaise, great uneasiness and restlessness, anorexia—*all positive evidences of the prodromal stage* of the disease. These symptoms may continue from three to eight days. The typical uneasiness referred to the throat and mouth begins before the end of the first stage.

The second stage, or period of excitation, is associated with spasms, pain in the throat—the latter promptly provoked by the attempt to swallow liquids—alarming dyspnea, cyanosis and irregular breathing, due to spasm of the respiratory muscles.

The frequency of the spasms increases as the disease advances and the true *"phobia"* is fully established; the sight of fluid, the noise of running water, the touching or moving of the patient, any jar, noise or the passing of a light are each sufficient to provoke spasms. The intervals between the spasms grow shorter, and the patient cannot be nourished; there may be slight *febrile movement,* 100-103° F., occasionally higher (104-105° F.), the pulse grows small and rapid and after from one to three days of spasms varying in different cases and during which death may occur, the majority of patients fall into the *third stage* or *stage of paralysis,* in which the weakness is overpowering.

There may be *paralyses* (usually of the extremity bitten) at times *hemiplegia,* or in occasional cases *ascending paralysis. Coma* develops and death results from *respiratory paralysis* in most cases; in some *syncope* suddenly ends life.

The duration of the *third stage* is from three to twenty-four hours. Death may occasionally follow the prodromal period without the symptoms of the second stage of the disease. The third stage (paralysis) promptly follows and is of short duration.

Conclusions.—From the foregoing abstract of symptoms and the course of the disease as presented in its three stages, it is clear that the *prognosis is absolutely bad in all cases of fully developed hydrophobia. Occasional cases have been reported cured,* in which it may be assumed that the diagnosis rested on a doubtful foundation. I feel justified in repeating that *the hope of the subject actually infected lies in the prompt cleansing of the wound and the early prophylactic treatment mentioned (the latter is now readily obtainable); that the greater the laceration of tissues and the deeper the bite, the greater is the danger of rabies developing.*

The Pasteur treatment requires three weeks, during which, at inter-

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vals, the patient is inoculated with the virus of rabies (dogs) which has been modified by the repeated inoculation of rabbits. The *antirabic* material is an emulsion of the spinal cord of the inoculated rabbits and to be effective the prophylactic treatment must have been completed at least two weeks before the end of the period of incubation.

Statistics.—Statistics prove further that of those bitten by rabid animals only 0.5 to 1 per cent who have been treated prophylactically, develop rabies, against 15 to 20 per cent among the untreated.

Reference

Romberg. *Die Acuten Infectionskrankheiten von Mehring u. Krehl. 8. ed.*

XVII. Dengue

(*Breakbone, Dandy Fever*)

Dengue is a rare disease except in tropical and subtropical climates. It is *acute and of unknown origin*, characterized by sudden onset, severe pains in joints and muscles, *fever with cutaneous erythema*, and characteristic *stiffness of gait* ("dandy gait"). It is usually *panepidemic or epidemic*, attacking a large proportion of the population suddenly. It is rarely found above the 41° north latitude, and Manson has expressed the opinion that the disease follows slowly along the lines of sea travel. The disease is likely to attack entire families, all under a single roof, and spreads from house to house along the same street.

While the specific germ is unknown, Ashburn and Craig proved that the disease is conveyed by the *mosquito* (Culex fatigans). (Investigations regarding the Etiology of Dengue Fever, 1907.)

There have been no epidemics in the Northern United States. The last large epidemic in America was in 1897 when 20,000 of Galveston's inhabitants were stricken, with practically no deaths. In a limited epidemic in Charleston in 1828, three deaths were reported.

From the above data it is clear that the *prognosis is good* and that *complications are exceedingly rare. Convalescence* may be slow, associated with prostration and weakness, with a persistence of erythema, and at times marked inertia and mental torpor. These symptoms yield fully, though considerable time is often required for full restoration to health.

The average *length of the attack is from seven to eight days.*

Immunity is of short duration, averaging about twelve to fourteen months.

Reinfection during the same epidemic has been noted by several clinicians.

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Section II

Diseases of the Respiratory Apparatus

A. Diseases of the Nose

1. Acute Catarrhal Rhinitis

(*Coryza*)

Acute catarrhal inflammation of the nasal passages is either a *primary infection* characterized by all of the usual changes in the mucosa of catarrhal disease, in which the secretion is materially increased, and finally purulent, or *secondary* to other infections, oftener in children with measles, whooping cough, bronchitis, laryngitis, syphilis, scarlet fever, diphtheria, or it may follow the use of the iodin compounds in both children and adults (often with idiosyncrasies).

Children suffering from *hereditary syphilis* are particularly subject to continuous *snuffles*, as are also those of *lymphatic temperament*, who on the slightest exposure are liable to contract "cold."

Both adults and children are subject to "colds" which are transitory as a rule, and without complications lead to recovery in a few days.

Most *secondary* (*infectious*) *rhinitides* are associated with more or less *pharyngitis;* the constitutional symptoms and gravity depend entirely on the nature of the primary disease. In all uncomplicated rhinitis the disease is self-limited, and does not materially interfere with the patient's activities. With grippal infection, scarlet fever, diphtheria and nasal involvement, extension to the surrounding sinuses is possible. With invasion of the middle ear, there may be mastoid suppuration or final pyogenic disease of the brain (meningitis, encephalitis, invasion of the veins, etc.). In children, neglect, particularly during periods of influenza, may lead to extension into the air passages, and final bronchopneumonia.

Much depends upon the resistance which the subject offers to the

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infection as well as its malignancy. With diphtheria, nasal and glandular involvement is always serious (See Diphtheria).

Syphilitic coryza in children—non-malignant—usually yields to treatment. If the deep structures are involved, recovery is naturally slow (See Syphilis).

Polypoid growths in adults often continue catarrhal discharges which are relieved by radical treatment. There are adults who develop ***nasal catarrh*** on slight cause, in whom there is also *asthmatic breathing.* Unless there are local disturbances, these symptoms are dependent upon neural or constitutional causes—and the prognosis should be given accordingly.

Catarrhal conditions of the nasal mucosa are often continued by pharyngeal adenoids. In these cases, usually children, the removal of the succulent growths brings relief. These patients are always worse during wet seasons. Children with lymphatic enlargements (cervical) and nasal catarrh dependent upon local lesions demand prompt attention, and are cured by modern radical treatment. The recurrence of coryza in the hypersensitive adult and child is favorably influenced by treatment which increases resistance.

2. Hay Fever

(*Rose Cold, Autumnal Catarrh*)

Most cases of hay fever are found in subjects who are predisposed to catarrhal disturbances, who have an abnormal and sensitive naso-respiratory mucosa. The leading clinical features of hay fever which follow the action of the pollen of certain plants, grasses, or the inhalation of irritating dust, are catarrhal and spasmodic. The *catarrhal symptoms* include coryza, free discharge, conjunctivitis; the *spasmodic,* repeated sneezing and asthmatic attacks.

Naturally the pollen of a certain plant being the cause of the symptoms in the individual case, the onset of the symptoms corresponds with its appearance in the air, and the release must be materially influenced by its disappearance and the immunity which it produces. The latter is short lived and questionable.

The prognosis of hay fever for life is good—it is self-limited and subject to recurrence. *Complications* are exceedingly rare. Occasionally, for some reason, without change of climate during subsequent seasons of pollen irritation, the complex does not return. There are probably no cases of rose cold which are not favorably influenced by climatic change. I have never met a death directly traceable to autumnal catarrh, nor a single extension to the air cells to cause bronchopneumonia. The asthmatic breathing and paroxysms disappear with the nasal symptoms.

Emrys-Roberts has demonstrated an interesting blood picture in con-

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nection with hay fever and asthma, which includes *increased eosinophilia coincident with the asthma.* He believes that there is an alteration in the blood picture, which besides the eosinophilia includes a *decrease of hemoglobin, marked polycythemia,* and *increase in large mononuclear lymphocytes, the presence of vacuolated* and *degenerated leukocytes* and a *degree of leukopenia.* "An altered, but modified blood picture persists during the intervals between the seasonal attacks."

Occasional cases have been benefited by the surgical treatment of local anomalies; considering the number treated, the results so far as the relief of nasal and respiratory symptoms during the periods of exacerbation, have not been encouraging.

The influence of vaccination against hay fever is at present *sub judice;* its influence on the control of the disease cannot be decided without further investigation. Lowdermilk claims good results from the use of toxin extracted from pollen with the addition of an autogenous vaccine, in all cases complicated by the presence of a bacterial infection (Freeman, I.).

Dunbar's investigations justify the use of his pollantin; if his conclusions are correct, relief and a moderate added immunity ought to follow. In the majority of cases it will be found that at present we have no remedy which positively aborts the symptoms. *Cocaine, used by physicians or patient, can only lead to temporary relief and encourages the formation of an enslaving drug habit.*

3. Epistaxis

(*Nosebleed*)

Nosebleed which is not due to mechanical insult (traumatism) is dependent upon *lesions of the nasal mucosa* (ulceration, catarrhal inflammation, dilated or diseased veins) or it is *secondary* to constitutional defects, including the hemorrhagic diathesis, purpura, scorbutus, hemophilia, the grave anemias, leukemias, carcinomatosis, malignant and non-malignant infections, sepsis, malignant endocarditis, typhoid fever, yellow fever, measles, smallpox, scarlet fever, pertussis, icterus and various poisonings.

Nosebleed is often an early evidence of arteriosclerosis, it may recur repeatedly with this condition; particularly does this happen with associated interstitial nephritis and hypertension. It may prove a salutary warning; slight bleeding with uncomplicated arteriosclerosis is insignificant.

Nosebleed is a frequent symptom of *heart lesions* and *cirrhosis,* or other *liver* lesions.

Epistaxis is not to be considered pathologic if moderate, when sudden changes to a high altitude cause it. Occasionally nosebleed may be an

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expression of *vicarious menstruation* and is of no importance. The significance of nosebleed which is secondary to the conditions above mentioned has been fully considered in connection with the separate infections; with malignancy it is always grave, also with the constitutional diseases and grave anemias.

Nosebleed *per se* does not often threaten life. In the exceedingly weak, with hemophilia, grave anemias, severe and uncontrolled bleeding does occasionally hasten death. Children during the period of growth, very often have recurring nosebleed which ceases at puberty; it is without significance. With the diseases of the ductless glands I have occasionally found insignificant nosebleed; one of my cases of acromegaly had frequent recurrences without ulcerative changes in the mucosa.

B. Diseases of the Larynx

1. Acute Laryngitis

Acute catarrhal laryngitis may be either *primary* or *secondary.*

Primary laryngitis is rarely associated with significant constitutional symptoms; occasionally there may be slight elevation of temperature, but this is evanescent, and barring the discomfort due to the changed larynx, hoarseness and cough, there are no evidences of illness. Such laryngitis runs its course in a few days to a favorable termination. Most cases show some associated inflammation of the trachea. When the larynx is inflamed from *strain,* the symptoms disappear after a short period of laryngeal rest.

The severity of laryngitis which is *secondary* depends entirely on the primary cause. With *corrosive poisoning,* edema may promptly follow or the swelling may be sufficient to cause asphyxia. Life is threatened; prompt surgical or local relief is demanded in such cases.

The *acute laryngitis of croupous diphtheritic origin* is separately considered (See Diphtheria).

With *measles,* in occasional cases, laryngo-tracheitis causes alarming symptoms which may be complicated by bronchopneumonia. Without the latter complication most of these children recover (See Measles and Bronchopneumonia).

Acute laryngitis with edema following fracture of the larynx or other *wounds* may prove dangerous. *Foreign bodies* caught in the larynx may cause laryngitis and *obstructing swelling.* These conditions are within the domain of the surgeon, who with modern devices succeeds in relieving most of them.

Primary or secondary *catarrhal laryngitis in children* often causes

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symptoms of croup and is known as "catarrhal croup" or "Pseudocroup." It is as a rule found in children who are subject to catarrhal laryngitis, and who whenever they "catch cold" are "croupy." In some there is slight elevation of temperature. This condition, when uncomplicated, is relieved in a few days after a period of cough, hoarseness and nocturnal increase of symptoms. *Sudden increase in the frequency of the respirations with rising temperature and pulse, create the suspicion of complicating bronchopneumonia.*

The *laryngeal picture* of *laryngitis*, when uncomplicated, will prove reassuring and is an aid in foretelling the course of the disease—also in diagnosticating the *subglottic form*, which may prove serious. The improvement of the general condition of the patient, the relief of associated lesions of the *nasopharynx* or other inflammatory conditions in the upper air passages, the relief of a rheumatic diathesis when present, favorable housing, climatic conditions (environment)—all prove powerful factors in not only relieving these patients in the acute attacks, but in preventing their return and final chronic laryngeal change.

2. Chronic Laryngitis

Chronic laryngitis is either *primary* or *secondary.*

The cases which follow repeated acute attacks (primary) can only be cured by long periods of rest, often climatic changes.

Chronic primary laryngitis due to the continuous inhalation of dust, tobacco or other irritating substances, if unrelieved leads to organic changes in the vocal cords, which continue annoying. None of these cases are relieved if repeatedly subjected to the factor which causes them. Laryngologists are agreed that but few laryngitides of the chronic type are primary, "except from the improper use of the voice" (Ballinger).

Secondary laryngitis may be due to nasal, nasopharyngeal or tonsillar disease. Removal of the primary lesion acts favorably on the laryngeal changes.

Chronic gastritis due to alcohol is frequently associated with chronic laryngitis, as are also *cirrhosis of the liver, chronic gastroduodenitis, heart lesions* causing venous enlargement, *mediastinal growths* of *Hodgkin's and leukemic origin and long residence in an unfavorable climate.*

The prognosis in all of these cases necessarily depends upon the depth of the change (hypertrophy, atrophy, polypoid or other productive lesions) and the ability to remove the underlying cause in the individual case.

The *voice* in chronic alcoholics who have had long-continued symptoms often remains hoarse in spite of the discontinuance of stimulants.

Pulmonary tuberculosis and *chronic bronchitis, chronic interstitial pneumonia* (the pneumoniokonioses) may be complicated by *non-tuberculous* chronic laryngitis—persistent and often unyielding to treatment.

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3. Edema of the Larynx

(*Edematous Laryngitis, Edema of the Glottis*)

Primary laryngitis may cause marked edema of the larynx. As a rule edema of the larynx is *secondary* to vascular obstruction, dependent upon the pressure of *growths*—malignant or non-malignant (cervical-mediastinal, etc.); *heart, kidney, lung lesions, constitutional diseases—diabetes, syphilis, the grave anemias* (*pernicious and leukemic*), *also purpura.*

Syphilitic tuberculous ulcerations may cause edema of the larynx. The general dropsies of *nephritis* at times include sudden edema of the glottis.

Peritonsillar suppuration (quinsy) may suddenly cause edema of the glottis, as may other infections which cause cellulitis or perichondritis, including erysipelas, Ludwig's angina, and malignant growths of the neck.

With measles, typhoid fever, scarlet fever, diphtheria or other infections, the glottis may become edematous; life is always threatened when such edema exists—it causes acute and alarming symptoms, whether dependent upon grave underlying causes or conditions which uncomplicated do not threaten life. This is particularly true of *angioneurotic edema* (Quincke's disease) separately considered. We have seen one case of diabetes in which there was one-sided swelling of the larynx, demanding immediate operation.

Edema due to injury, foreign bodies and surgical affections is mentioned in connection with the laryngitides.

The laryngoscope leads to the recognition of the extent of the danger and often suggests treatment which prevents fatal asphyxia. The immediate prognosis for life must always depend upon the ability to overcome the obstruction and prevent recurrence. Our art (laryngology) is so far advanced that whatever the primary cause, but few will lose their lives from the edema itself who are treated early and rationally.

The organic diseases of the vital organs which serve as the most frequent cause of edema of the glottis usually terminate fatally.

4. Laryngismus stridulus

(*Spasmodic Laryngitis*)

The "holding of the breath" by the child is the characteristic feature of laryngismus stridulus. Spasm of the glottis may be caused by a variety of laryngeal and nervous disturbances. It is an affection of the nervous system of infant life (6 months to 3 or 4 years) and is often provoked by emotional causes. Children often while crying "hold their breath" without any serious result. I consider spasm in connection

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with tetany and infantile convulsions, to which section the reader is referred.

The majority of my cases have been found in children with neurotic tendencies, rachitic, underfed, and emotional. Some of these show the characteristic reactions of *tetany*. The spasm involves the diaphragm as well as the adductors of the larynx and for the fraction of a minute the appearance (cyanosis) alarms the parent. The inspiratory stridor which follows is always welcome to the over-anxious observer. Probably the deaths which have been attributed to laryngismus stridulus are chargeable to the *status thymolymphaticus*. I have never in our practice seen a death from laryngismus stridulus.

Adult stridulus is occasionally met in practice; it may be hysterical or evidence of another neurosis. It is not serious.

The *laryngeal crisis* of *tabes dorsalis* includes characteristic stridor and may recur at short intervals without serious result.

Mueller (Fr.) claims that in rare cases laryngeal crises may cause sudden death by asphyxia.

5. Tuberculous Laryngitis

See Tuberculosis, Section I, B.

6. Syphilitic Laryngitis

See Syphilis, Section I, A.

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C. Diseases of the Bronchi

1. Acute Bronchitis

Acute bronchitis is one of the most frequent of all diseases, at the same time one of the most benign. It is easily the most frequent of all diseases of the respiratory tract. The majority of acute cases are *primary*, more frequent during the fall and winter months—always mate-

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rially influenced by sudden climatic changes and exposure. In otherwise healthy subjects, without added complications, it offers an absolutely favorable prognosis.

Many acute bronchitides begin as laryngeal or pharyngeal catarrh and descend after a day or two of local symptoms.

Bronchial Catarrh.—Bronchial catarrh is associated with more or less tracheitis. The bronchi are symmetrically inflamed (both sides) and the medium-sized bronchi are mainly involved. The bronchitis of early life and old age when neglected or extensive is likely to extend to the smaller bronchi; hence it is always serious and there is great danger of *secondary bronchopneumonia.* The *bronchiolitis* of early and late life is often *secondary* and is a complication of influenza, measles, whooping-cough, diphtheria and other infections.

When in the young or old, bronchopneumonia develops with bronchiolitis, or disseminated bronchitis extends to the capillaries and air cells, an enormous element of danger is added. (See Bronchopneumonia.)

The prognosis of bronchopneumonia following the bronchitis of measles and whooping-cough is always grave (see Measles and Whooping-cough), particularly in very young and feeble children.

Atelectasis—collapse of air cells—is one of the serious complications of bronchiolitis and bronchopneumonia. With bronchiolitis or fully developed islands of bronchopneumonia, and extensive collapse of air cells (atelectasis) the condition of the patient is always serious—*marked cyanosis* and *cardiac insufficiency* may end the scene.

Whenever with acute bronchitis there is *persistent high temperature* and *respiration is correspondingly accelerated*, the possibility of *complicating pneumonia* should be considered.

In uncomplicated bronchitis the acute symptoms begin to yield on the third or fourth day; the expectoration becomes more profuse and purulent; the acute symptoms (malaise, slight fever, anorexia and cough) show marked improvement, and uninterrupted return to health is the rule.

Dyspnea and *rapid respiration* in all cases when present demand immediate interpretation; they are not symptoms of uncomplicated bronchitis.

Cough may not cease entirely before the end of the second week. If it persists beyond that time and there is some evening temperature, with or without acceleration of the pulse, the suspicion of a tuberculous infection in the absence of other infection or cause should be strongly entertained, and the case treated (watched) accordingly.

Heart weakness in the aged and infants with disseminated bronchitis is always of serious import.

Primary uncomplicated bronchitis in otherwise healthy individuals always leads to recovery. The *virulence* of primary infections with which bronchitis may be associated must always be considered to be of paramount importance.

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Acute bronchitis, complicating chronic heart lesions, nephritis or other visceral diseases may seriously influence the prognosis. The prognosis in these cases depends largely on the general condition of the patient, the resistance and the extent of the bronchial infection. The same is true of bronchitis as it arises suddenly with cerebrospinal meningitis, polyarthritis, coronary disease, pulmonary emphysema, mitral lesions, rachitis, sepsis, typhus and smallpox.

2. Chronic Bronchitis

Chronic bronchitis may follow acute catarrhal bronchitis. As a rule, chronic bronchitis depends upon long-continued hyperemia of the bronchial mucosa which is secondary to pulmonary obstructions and dependent upon valvular lesions, weakness or disease of the right ventricle, pulmonary emphysema, the pneumonokonioses; particularly the inhalation of dust laden air. With chronic bronchitis there is but little tendency toward return of the membrane to a normal state. While the atrophic or hypertrophic changes are not overcome, life may not be threatened, for some of the patients live to reach old age and many die of intercurrent disease.

Bronchiectasia and *bronchial stenosis* may result from long continued bronchitis. Chronic bronchitis is a frequent cause and accompaniment of *pulmonary emphysema.* With this complication the right heart is overtaxed, and finally dilates and hypertrophies.

There are forms of chronic bronchitis which are materially affected by seasonal and climatic influences. Thus with "*winter cough*" the patient may cough or have symptoms only during cold weather, and is promptly relieved by climatic treatment. Most chronic bronchitis is favorably influenced by warm weather or by a dry equable climate.

There are cases in which *chronic change in the mucosa causes an excessive mucopurulent secretion with cough and final secondary heart and trophic changes*—clubbed fingers (See Chronic Pulmonary Arthropathy). These cases are exceedingly chronic; they are types of *bronchorrhea.* In these as in most chronic types of bronchitis there is more or less peribronchial proliferative change. *The dry bronchial catarrh of Laennec* is at once exceedingly troublesome and chronic, because of the persistent dry cough, with only the occasional expectoration of a small pearl-shaped plug and the secondary heart changes, emphysema with dyspnea, which are practically uncontrollable.

Chronic bronchitis dependent upon chronic heart lesions is often materially relieved during long periods by the improved condition of the myocardium. But few of these cases cease coughing entirely during the periods of improvement, but they remain comparatively comfortable. In a large number, the cough with excessive expectoration (bronchorrhea) con-

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tinues without materially interfering with the general condition of the patient. The primary disease always determines the outcome.

Any form of bronchitis may be associated with *asthma*, and in most, *emphysema* is more or less developed.

While as above stated chronic changes in the bronchi do not tend to mend, the outcome so far as life is concerned is not discouraging, save as it is influenced by the primary circulatory or other faults which cause the disease, or by the secondary lung or heart changes which the bronchitis itself produces.

Chronic bronchitis with *"fixed thorax"* may be materially improved in well selected cases by plastic operations on the thorax (See References).

Chronic purulent bronchitis with asthma (*purulent bronchorrhea*) *and emphysema* may be associated with polypi, adenoids, or nasal perforations; while the majority are not cured by radical surgical treatment of the nasopharyngeal anomalies, many are materially relieved. Climatic and seasonal changes influence these cases favorably.

Chronic putrid or fetid bronchitis is secondary to gangrene of the lung, empyema, tuberculosis, syphilitic or malignant disease. These cases are not curable; the length of life is measured by the primary cause and its extent. Distant secondary changes (metastases) may promptly end life (brain abscess, infarct, amyloid disease, etc.).

3. Bronchiectasis

Dilatation of the bronchi may be either (1) *congenital* or (2) *acquired.*

(1) The **congenital type** (Grawitz) (bronchiectasis universalis) is exceedingly rare. Most congenital cases have been found to be unilateral. There is no treatment which influences these defects; the amount of disturbance and influence on the life of the child depends upon the extent of the bronchiectasis. In those who live, secondary pulmonary and heart changes must be expected.

(2) The **acquired brochiectasis is** *always secondary.* Reference is made to bronchial dilatations in connection with infectious pulmonary diseases and chronic bronchitis (See separate sections).

Classification.—Barty King classifies the acquired bronchiectasis as follows:

- Bronchiectasis
  - A. Pure
    1. Chronic bronchitis.
    2. Bronchopneumonia.
    3. Chronic pneumonia.
    4. Pneumonic.
    5. Pleuritic.
  - B. Tuberculous.
  - C. Traumatic
    1. Aneurism.
    2. Tumor.
    3. Foreign body.
    4. Syphilis.

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All bronchiectases are either (a) diffuse or cylindrical, or (b) circumscript or saccular.

(a) The *diffuse or cylindrical forms* are not as a rule extensive.

(b) The *circumscript or saccular forms* are either single or multiple.

In severe cases a section of the lung shows the appearance of innumerable saccular dilatations resembling multiple cavities.

Symptoms and Course of Complication.—The symptoms and course of the complications *depend on the size and number of the bronchiectatic cavities,* the *character of their contents* and the *amount of constitutional disturbance caused by absorption and the nature and extent of the primary lesion.*

Causes and Development of Bronchiectasis.—The most frequent cause of bronchiectasis is chronic inflammation of the bronchial wall which is associated with or is a sequel of measles, whooping-cough and influenza—usually during early life. A large number of bronchiectatic cavities which develop during early life increase in size with advancing years. In these cases the walls are thickened by growth of connective tissue. With chronic bronchitis there may be no advance in the size of the cavities or there may be diffuse dilatation of many bronchi which increases (Aschoff). With pressure from *tumors* or *stenosis* due to the presence of a foreign body, syphilitic cicatricial tissue following ulceration, tuberculous ulcerations or aneurismal growths, the cavity, one or many, may increase and the symptoms are correspondingly aggravated.

Associated Symptoms.—*Atelectasis and bronchiectasis* may be associated conditions. If the former is extensive and arises suddenly, the dangers are at once apparent because of cyanosis, respiratory and circulatory embarrassment. In children and in the aged with bronchopneumonia, *acute bronchiectasis with or without atelectasis* is always serious and usually leads to death. The symptoms which are associated with good sized dilatations are characteristic. Cough may be absent during the larger part of the day, troublesome early in the morning when it is accompanied by the emptying of the pocket which brings relief. The size of the cavity may be approximately decided by the quantity of secretion (expectoration) which it holds.

The *complications* depend, as already hinted, upon the primary causes and the changes consecutive to the dilatations—local and constitutional.

The average chronic case without excessive and multiple dilatations lives on, never without some symptoms, but in fair health; not a good subject for added infection—pneumonia particularly. With *extensive and multiple dilatations and excessive purulent secretion,* with *fetid expectoration* the prognosis is always grave. Patients with febrile movement after many years of invalidism become septic, develop anemia (secondary), are exhausted and emaciated, and often die with advanced amyloid degeneration in many organs. We have seen cases, particularly syphilitic, re-

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main stationary and in good general health after intensive treatment during many years.

4. Bronchial Asthma

Bronchial asthma is a neurosis, usually of reflex origin; characterized by paroxysmal dsypnea, narrowing of the bronchi by *spasm, hyperemia* or *exudation;* commencing suddenly, as a rule; soon accompanied with loud wheezing breathing, spasmodic cough, prolonged and defective expiration, in which the respiratory muscles are all overtaxed, the lung is distended, expectoration is usually profuse, there is associated bronchitis and emphysema, and in chronic cases changes in the heart, thorax and blood—all of these symptoms are without attending fever.

Charcot-Leyden crystals (small colorless octahedra) are found in the sputum in most cases and are not of prognostic significance, neither are the Curschmann spirals. Curschmann considered the presence of the spirals as positive proof of inflammation of the finer bronchi (bronchiolitis exfoliativa). The presence of blood in the sputum is not necessarily or usually ominous; in the severer attacks the sputum is at times bloody. Large hemoptysis is not a symptom of primary asthma. Eosinophilic cells. usually present in the sputum, are of no prognostic significance. The individual attack may end in less than one hour; as a rule it continues several hours (2 to 4). Severe attacks may continue during several days with only slight and not complete remission.

Meltzer in 1910 called attention to the resemblances of asthma to anaphylactic shock and offered the suggestion that "it is an anaphylactic phenomenon." Certainly there are a number of facts which strengthen the theory of Meltzer, particularly those which prove the frequency of recurrence under similar conditions and exposure to the same causes which prove hypersensitivness, abnormal reaction, or as Meltzer says "asthmatics are individuals who are sensitized to a specific substance."

The disease is not fatal *per se.* There are facts which prove the enormous influence of a *psychic element* in inviting and continuing symptoms, particularly in neurotic individuals in whom no organic lesion can be found. In some cases suggestion has been powerful in determining the onset of attacks. West mentions the presence of premonitory symptoms which if heeded may abort or prevent the paroxysm—"like the aura in epilepsy."

Trousseau a sufferer from bronchial asthma had his attacks with great regularity "as the clock struck three in the morning."

One attack usually leads to more; it is unusual to find one attack the only paroxysm during the entire life of the patient. The more frequent the attacks, the lighter they are, as a rule, though there are exceptions to this. Postponing of attacks or increasing the length of the intervals is

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favorable and in some cases such behavior is followed by almost complete immunity.

Heredity.—Heredity is a factor of some importance in connection with prognosis. It is noted in about 2 of 5 cases. Salter's statistics in 217 cases showed 84 with a strong heredity, and often direct from parent to child and through several generations. Salter and West report the occurrence of asthma among several children of a family without the disease in the parent. The prognosis for complete relief is better in the cases without inherited taint.

Sex.—Salter's statistics show 153 cases of which 102 were males, and 51 females.

Age.—Asthma in young children often disappears after one or more attacks. Salter offers the following table to show the age at the time of the first attack in 225 asthmatics:

During	1st year	11 cases	31. per cent.
	1–10 years	60 cases	
	10–20 years	30 cases	12.8 per cent.
	20–30 years	39 cases	17. per cent.
	30–40 years	44 cases	19. per cent.
	40–50 years	24 cases	9. per cent.
	50–60 years	12 cases	5. per cent.
	60–70 years	4 cases	1.4 per cent.
	70–80 years	1 case	0.4 per cent.

Salter says that the chances of cure are good when asthma develops before the age of 10 years; if before 20 it may be cured; if between 20 and 40, it will probably not be cured; if after 60 it will certainly not be cured.

Occupation.—Occupation is not of as much importance in etiology or prognosis as is generally supposed. Those most exposed are not likely to develop asthma unless they are predisposed and work in an atmosphere of dust. It has seemed that those who use their voices most are subject to asthma (preachers, lawyers, school teachers, etc.) but this remains without confirmation. Once present, occupations which continue irritating, provoke seizures and prevent long periods of immunity.

Additional Influences and Symptoms.—*Gouty and diabetic families* show a surprisingly large number of asthmatics, and in these the prognosis for complete freedom is not encouraging. In young children *the association of intractable eczema and asthma* is striking and frequent. A number of our cases with this combination proved subject to pneumococcus infection. In one child we had, as a complication, four threatening bronchopneumonias during four consecutive winters. This boy has grown to manhood cured of both asthma and eczema. Another active chap with the same clinical picture, was less fortunate; he died in his third bronchopneumonia.

Asthma is comparatively frequent with urticaria. Bulkley's figures

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are high (7 per cent). Asthmatics both young and old, are as a rule, unusually *active* and *alert* and when at work are *strenuous.*

Location and climatic conditions are of great importance in most cases but there are absolutely no indications which the individual case offers which can lead the clinician to determine the location or climate which will most favorably influence the majority of "idiopathic asthmas." Most asthmatics, it may be safely concluded, are favorably influenced by change to a higher altitude, particularly if they are living in the lowlands. Patients are able to get some relief from *postural change,* particularly by raising the shoulders and the scapulæ. Clavicles and spine are fixed, the patient leans forward, the back is curved, the head rests on the hands, the anteroposterior diameter of the chest is increased while the diaphragm is depressed and the respiratory effort is extreme as it raises the ribs. The respirations are long, noisy, wheezing, though not abnormally rapid. Profuse expectoration gives considerable relief, while in the more troublesome attacks the sputum is scanty and the asthma "dry."

Blood Picture.—The leading characteristic of asthmatic blood is eosinophilia. *The eosinophils are often increased to from* 10 *to* 40 *per cent of the leukocytes.* Higher counts are recorded. Early in the attack the eosinophils are usually reduced but soon there is a decided increase; with the decrease of eosinophils early, there is a lowering of the lymphocytes and the polymorphonuclear cells increase. Later in the attack there is evident eosinophilia, as suggested above with marked lymphocytosis, all of which fall as the attack is relieved. Asthmatics often show persistent lymphocytosis. But little of value for prognosis is gained from blood examination though in the terminal stages of some secondary asthmas (heart and pulmonary lesions) *polycythemia* may be present.

General Considerations.—I have elsewhere mentioned the paroxysmal breathing, cyanosis, and asphyxia which lead to sudden death (*thymic death*) now known as the *status thymo-lymphaticus.* This is not to be confounded with bronchial asthma.

Cardiac asthma is usually a terminal symptom of *heart* or *cardiovascular disease* in which *myocardial degeneration* is the prominent feature and in which *pulmonary edema* is likely to lead to death.

Renal asthma is not unusual with nephritis in which the heart muscle is advanced in degeneration and uremia may be chronic or acute. The heart is erratic, feeble and arhythmic, and with increasing evidences of cardiac and respiratory insufficiency—pulmonary edema—death follows. There are cases dependent upon gastric or gastro-intestinal or hepatic disease, either organic or functional. Many asthmatic paroxysms may be traced to faulty digestion or organic disease of the digestive apparatus in which diet and radical treatment exert a marked and favorable influence on the asthmatic attacks. When asthma is symptomatic of grave organic disease (cardiac, renal, pulmonary or gastric) the prognosis is bad; this,

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however, is not veritable asthma. *Spasmodic or bronchial asthma* which is a neurosis as originally defined in this chapter, is the only variety which should be included in the consideration of true asthma.

With vagotonia of Eppinger and Hess (see Diseases of the Sympathetic System) the subjects develop asthma with the other symptoms included in the complex (increased susceptibility to pilocarpine, nervous dyspepsia, hyperacidity and erratic heart) and are materially relieved by adrenalin. As in hay fever, so in vagotonic asthma the eosinophilia is characteristic.

There are occasional asthmas which seem reflex from some genito-urinary disturbance. Menstrual anomalies, pregnancy and uterine displacements in the female, and sexual disturbances and neurasthenia in the male have occasionally been considered among the causes. Most of these patients are neurotics and are influenced by suggestion rather than by radical treatment in most cases.

There is practically no danger to life during the attack. *There are so few cases recorded in which death occurred during an attack that it may be safely assumed that in these there was some complication.* Fagge, Franzee and Bamberger each report one case of death during the asthmatic attack. Asthma does not *per se* shorten life. It has been noted that *asthmatics often live to old age.* I saw the case of a salt boiler who had asthma over 60 years and died at about 90 years of age. In *chronic asthmatics* with marked secondary changes including *emphysema* and *heart lesions* (dilated right ventricle) life may be shortened by such complications. In *young subjects and in the aged* there is danger from *bronchopneumonic infection.*

The *association of asthma and tuberculosis* is strikingly rare, though in some cases the x-ray shows calcified and tuberculous glands in asthmatic subjects (Fr. Mueller). When attacks increase in frequency and severity at the same time and their length increases, the chances of cure are remote. The chances of relief are increased by decreasing severity of the attacks and lengthened intervals. The positive discovery of the cause of the reflex materially improves the chance of amelioration or cure. I have often been disappointed by radical nasal treatment in cases which seemed to depend upon nasal growths or other anomalies, though occasionally success either complete or partial has followed.

West says: "Although it is clear from what has been stated that there is more in the relation of nasal irritation to asthma than has been until recent years believed, and although most marked relief is given in some cases, still so far as we know at present it is impossible to recognize beforehand with certainty the cases in which relief will be given and those in which it will fail." The conclusions of West are sound and safe to follow in offering a forecast in those cases in which some nasal abnormality seems to be the irritant.

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Asthma sometimes disappears after intercurrent disease or it may alternate with other and graver diseases of the nervous system. Salter, Lloyd, and Taylor report cases in which *asthma alternated with epilepsy;* Trousseau reports the cure of *asthma after gout* but persistent *hemicrania followed.* Eulenberg records a parallel case in which asthma alternated with *hemicrania* and *angina pectoris.* Savage and Conolly Norman prove the relation between *asthma and insanity;* the two affections alternate at times. There was freedom from asthma so long as the insanity continued; on cure asthma returned.

Long-continued asthma, while it does not, as already suggested, shorten life without some added complication, in the advanced stage may lead to the *"fixed thorax" with emphysema* and all the associated physical signs. In these cases dyspnea may finally be continuous and with heart changes, dilatation of the right heart, edema of the lung may develop and threaten life. I have seen two cases, in extreme condition, relieved by plastic operation on the thorax. The improvement of both was prompt and seems to continue. *But few chronic asthmatics are without evidences of incurable chronic bronchitis between their paroxysms.*

Secondary asthma depending on pressure of growths upon the pneumogastric offer no hope of relief. Among the most distressing cases of asthma are those due to metastases or primary growths (mediastinal). In many of these the dyspnea and cough are paroxysmal, the breathing noisy and characteristic of true asthma. In the terminal stages with these conditions the breathing is continuously bad with marked cyanosis.

To prevent serious accident or death the *anaphylactic action of diphtheria and other antitoxins administered to asthmatics* demands serious attention in the presence of the diseases for which these are used.

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5. Fibrinous Bronchitis

(*Croupous Bronchitis*)

Fibrinous bronchitis may be either *acute* or *chronic. When acute it is usually secondary and molds*—fibrinous casts of the bronchi—are formed because of descending croupous inflammation with diphtheria, occasionally with croupous pneumonia or any pseudomembranous disease of the upper respiratory organs. With all of these conditions extension into the finer bronchi and air cells with the formation of casts adds enormously to the danger of the primary disease. *Caustic poisons* may in rare cases cause fibrinous bronchitis. In occasional malignant neoplasms of the lung casts of the bronchi have been formed.

Primary fibrinous bronchitis is exceedingly rare. In an active practice of over thirty ears I have seen but one case. This was chronic; it commenced in a girl at the age of eight years. Casts of the bronchi formed without materially affecting her growth or general condition, varying at intervals during six years, after which she made a full recovery and has never, after thirty odd years, had recurrence. No treatment influenced this case; it ran its course and the habit of making casts was lost. This patient never had asthma during the active years of the disease.

6. Whooping-Cough

See Infectious Diseases (Section I).

D. Diseases of the Lungs

(The Pneumonias and Pulmonary Tuberculosis are considered in Section I—Infectious Diseases.)

1. Circulatory Disturbances of the Lungs

Congestion

(a) Active
(b) Passive
(c) Edema of the lungs.

(a) Active Congestion of the Lungs (*Woillez disease*).—It is questionable whether active congestion of the lung ever exists as an inde-

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pendent disease. Most of these cases have been strongly suggestive of *abortive pneumonia.* Woillez in 1854 called attention to *congestion pulmonaire idiopathique,* which develops after chilling of the surface (usually from a fall into cold water or injury of the thorax) and in which there is sudden chill, some fever, pleuritic pain, cough, dyspnea and expectoration which settles in two layers one frothy and yellowish, the other mucilaginous; usually there are pneumococci present. In occasional cases the expectoration is absent. The symptoms run a favorable course in four or five days. There is leukocytosis. The disease in rare instances runs a more protracted course but ends in recovery.

Active hyperemia not depending on pneumonia, with sunstroke, inhalation of poisonous gases or acute miliary tuberculosis is of no clinical importance (Staehelin), and of such rare occurrence that its occurrence is questioned.

(b) Passive Congestion.—Passive congestion of the lung may follow *mechanical obstruction* secondary to *tumor, insufficient heart force* or decompensation. The *condition is always secondary and serious because of the gravity of the initial disease.* In the *terminal stages of malignancy, constitutional diseases, the wasting and acute diseases of the aged,* with *valvular lesions,* most frequently *initial disease, chronic and acute nephritis, and purpura,* passive congestion may develop, and in some continue long enough to produce *brown induration* (Aschoff).

I have, with all primary disease to which passive pulmonary hyperemia may be secondary, dilated on its prognostic significance. Unless the circulation can be sufficiently stimulated or the pressure removed when present, the prognosis is absolutely bad.

The *suddenly arising engorgement of the pulmonary vessels with heart disease* is usually associated with edema (See heart lesions, also pulmonary edema). *Hypostatic congestion of the lung* is always secondary; it is a frequent attendant of all long continued infections and in these cases causes engorgement of the dependent portions of both lungs, as a rule. It is almost constantly present with pneumonia, severe typhoid infection, the infections of old age and early life; when in the latter they are serious when the patient has been kept on the back during long periods. Hypostatic congestion may prove a serious complication with fractures of the hip and other bones, particularly in delicate old and non-resistant patients. With marked dyspnea, cyanosis and weak heart, also with edema, the prognosis is grave.

Hypostatic congestion with the majority of infections does not lead to death or materially influence the chances of recovery unless it is extensive, and the heart is enfeebled by overpowering toxemia. *Postural change and other prophylactic treatment* do much to prevent the development and advance, when present, of the complication.

With *cerebral apoplexy, opium poisoning, brain tumor* and *other brain*

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lesions, uremia and a variety of *other unfavorable primary diseases* hypostatic congestion may prove to be the leading cause of death.

(c) PULMONARY EDEMA.—Edema of the lung is never to be lightly regarded whatever the primary condition which causes it. References to the clinical and prognostic significance of pulmonary edema are frequently made in all separate sections dealing with conditions which may cause it. There is no more alarming condition, none which demands prompter relief that life may be prolonged than that which presents when the patient is literally drowning in his own serum. I say "life prolonged" for in the larger number of cases pulmonary edema is secondary to grave conditions. On the other hand, *there are occasional edemas from which patients make full recoveries;* these are with such underlying conditions as can be relieved, or they do not recur. I have found among my favorable cases the *edema secondary to acute nephritis, to sudden cardiac insufficiency with acute infections, pneumonia, typhoid, measles, myocardial weakness* with *endocarditis and polyarthritis, specific aortitis, coronary sclerosis and myocardial degeneration;* in all of these active treatment proved sufficient to bridge the patient over the critical period.

The *unfavorable hypostatic congestions* are those in which the heart is so far degenerated or the toxemia so malignant that response to general and local stimulation is impossible. I have called attention (see Pneumococcemia) to those rapidly fatal cases of pneumonia in which the air cells are promptly filled with blood serum which in a few hours drowns the patient. With nephritis, heart insufficiency, arteriosclerosis, the prognosis in the presence of an acute pulmonary edema is bad. With angina pectoris and acute edema the chances of recovery are small. In many of these cases overeating is an important exciting factor of the attack.

With any heart lesion which leads to insufficiency—decomposition—the addition of edema is life threatening.

With *emphysema and heart (right) dilatation,* suddenly arising edema leads to cyanosis and often to death. These patients are usually among the more chronic and debilitated.

Sudden edema with obesity and fatty heart, is, as a rule, fatal. Angioneurotic edema may cause edema of the lung; it is rarely fatal—in fact it is not frequent. I have seen *epilepsy with edema* recover. *Any cause which weakens the left heart* sufficiently to interfere with the pulmonary circuit and cause edema, as already strongly hinted, unless promptly relieved will lead to death.

The *duration* of the single edema of the lung in severe cases cannot be long, for when severe, it is associated with such reduced myocardial strength that death is likely to follow soon. Pulmonary edema by rigorous treatment with fatal primary conditions may be overcome. It is likely to recur, and may finally claim its victim.

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2. Pulmonary Hemorrhage

(a) Hemoptysis
(b) Pulmonary Infarct

(a) *Hemoptysis*

Coughing or raising of blood from the air passages is symptomatic of many primary conditions; the most frequent cause of blood spitting is tuberculous disease of the lung (See Tuberculosis).

Hemorrhage from the pulmonary vessels may be due to traumatism when the nature of the injury and extent will make prognosis easy. *Active hyperemia* causing hemoptysis is inflammatory in most cases. The causes are acute pneumonia, tuberculosis, and Staehelin mentions malaria. With pneumonia we have never seen hemoptysis sufficiently profuse to deplete the patient or cause weakness. *The pure bloody sputum of pneumonia is not encouraging*—such complication is found in the graver cases. (There are occasional exceptions.)

The hemorrhages—*hemoptysis of malignant growths,* rarely cause serious weakness. In the terminal stage occasionally large vessels may be eroded, and weakness already extreme becomes threatening.

Vicarious menstruation may include hemoptysis which, aside from the psychic effect of the bleeding, is without depressing or weakening effect.

Ulcerative disease of the upper air passages, pharynx, larynx and trachea may cause slight hemoptysis. *Hemoptysis due to mitral stenosis* often relieves the patient's breathing; it rarely causes more than transitory weakness. In all such cases the possibility of tuberculosis should be considered.

Wilson has grouped his cases of hemoptysis in heart disease in three principal groups:

"(1) Those in which with an antecedent or concomitant lesion of the heart, the hemoptysis is essentially of pulmonary origin, as in tuberculosis, croupous and sometimes bronchopneumonia, infarct, acute and chronic bronchitis, emphysema, bronchiectasis and malignant growths."

"(2) Those in which vascular structures are the seat of hemorrhage, as aneurism, erosion caused by foreign bodies or malignant growths, and primary and secondary diseases of the blood."

"(3) Those which are primarily and essentially of cardiac origin."

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In the first two groups the prognosis is grave as the primary disease undermines resistance and the hemoptysis is profuse. In this chapter we consider the hemoptysis from many of the sources mentioned *without* associated heart disease, the latter naturally under certain conditions adds to the danger. With a good myocardium, and in the majority of cases because of the limited loss of blood, the prognosis is good so far as the hemoptysis is concerned, except in aneurism. All clinicians have noted that moderate hemoptysis in mitral stenosis is usually followed by material relief of dyspnea and other cardiac symptoms. Mackenzie says that with mitral stenosis "at various stages the patients may be seized with great bleeding from the lungs. There doubtless the cause is the back pressure in the pulmonary circulation and rupture of the blood vessels. As a rule, this is a grave sign, the patient dying sometimes shortly after the attack."

We have not often met these large hemorrhages with mitral stenosis. In most hemoptyses due to heart lesions the immediate prognosis is good; naturally the course of the disease is molded by the nature of the primary heart defect.

The *bleeding of pulmonary gangrene* is not as a rule profuse; in one case we saw a fatal hemorrhage—this is exceptional.

The slow bleeding of the *aortic aneurism* is ominous, while the *rupture of the sac* into the air passages is always promptly fatal. Aneurismal bleeding from whatever vessel into the bronchi, whether slow, sudden or profuse, leads to death.

With *chronic bronchitis* blood streaked sputum is frequent. Hemoptysis is rarely profuse. The admixture of blood is usually due to violent coughing. No significance need be given to this bleeding.

With *whooping-cough* and *measles* in children and adults during violent paroxysms, hemoptysis often occurs without influencing the general condition.

With *syphilitic ulceration of the upper air passages*, hemorrhage is not often severe. There is usually only a slight addition of blood (See Syphilis).

With *malignant purpura*, hemoptysis may be either slight or it may be profuse. When it is present it is only one of several complicating conditions with profound constitutional changes and should be accordingly interpreted (See Purpura; also Scurvy). Some cases which often look serious finally recover.

Hemophiliacs occasionally bleed freely from the bronchial mucosa, particularly when there are catarrhal or other inflammatory changes. The general and circulatory condition of the patient, the blood state, the nature of the primary disease, and the quantity of blood lost make prognosis possible and usually correct.

Hemoptysis with arteriosclerosis and chronic interstitial nephritis in gouty subjects particularly, will usually prove more alarming than serious;

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the underlying primary disturbances make prognosis possible. The loss of blood is not usually great.

Abscess of the lung rarely causes large hemorrhage; with a persisting cavity there may be repeated small hemorrhages. In these cases the blood and pus are mixed. These slight bleedings do not influence the course of the primary disease materially.

Profuse hemorrhage from any cause into the air cells may, particularly in patients weakened and reduced by chronic disease, lead to suffocation or heart weakness.

The *presence of blood in the lung may* by aspiration to distant parts of either lung—if it holds pathogenic germs (the pneumococcus particularly)—lead to acute inflammatory processes, just as, after pulmonary hemorrhage in tuberculosis, the bacillus and other microörganisms may be aspirated to dependent parts of the lung, and acute pneumonic tuberculosis may result.

(*b*) *Pulmonary Infarct*

(*Pulmonary apoplexy*)

Wedge-shaped (usually) or other infarcts into the lung tissue are dependent upon chronic heart lesions, malignant or septic infections with embolism or thrombosis of the pulmonary artery, mechanical obstruction from pulmonary or circulatory anomalies which produce the characteristic *"heart lung."* If the blood effused is not great, there may be but slight hemoptysis and few subjective or objective symptoms. In such cases the clot is finally expectorated as a black or dark purple airless lump (West, S.). If there is extensive infarct (malignant endocarditis and other septic conditions, chronic nephritis) an entire lobe of a lung is suddenly filled. It is impossible always to tell from the hemoptysis how extensive the infarct may be. I have seen large infarcts with but little blood spitting. In these cases the physical signs, dyspnea, and heart conditions decide the immediate prognosis.

Infarct of a large branch of the pulmonary artery or sudden obstruction with myocardial insufficiency (left ventricle) in which with hemoptysis the subjective symptoms are severe, promptly leads to death.

Pulmonary infarct may, after varying periods of hemoptysis, lead to *pulmonary gangrene* with change in the expectoration; these patients die with symptoms of sepsis. The conditions which lead to the majority of pulmonary infarcts are serious and are separately considered with the infections, heart and other lesions. There are many chronic heart and other lesions in which pulmonary infarcts do not lead to death; they may recur. We have, with chronic cases of malignant endocarditis had repeated hemoptysis due to infarcts from which the patients have rallied, to die of brain infarcts or other complications. Multiple infarcts are not infrequently found in many organs of the body, post mortem.

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3. Chronic Non-tuberculous Pneumonia

Included in this consideration of *Chronic Non-tuberculous Pneumonia* are:

(a) Chronic pneumonia.
(b) Chronic interstitial pneumonia.
(c) The pneumonokonioses.

(a) *Chronic Pneumonia*

There are occasional cases in which the exudate present in the air cells in the third stage of pneumonia remains unchanged and continues an irritant, producing changes which lead to chronic pneumonia. These are the so-called cases of *delayed resolution or unresolved pneumonias.* As already suggested (croupous pneumonia) *the majority of "unresolved pneumonias" prove ultimately to be tuberculous; they are cases of empyema, or the persisting symptoms are due to some other added complication.* It is however possible for delayed resolution or "unresolved pneumonia," either fibrinous or catarrhal, to lead to chronic, non-tuberculous changes in the lung. *The tendency is toward the proliferation of connective tissue and carnification.* There is, with both types of pneumonia which become chronic, more or less *peribronchitis* with the changes mentioned. It is impossible to differentiate these cases from *chronic interstitial pneumonia;* indeed, the pathology of both is identical when the disease is fully developed. Further references to the prognosis of chronic pneumonia are therefore included in this chapter.

Chronic pneumonia is usually the outcome of the atypical types of the acute disease; it often follows measles and whooping-cough in children who are burdened by diatheses (tuberculous or rachitis), and in all cases there is great danger of the ultimate tuberculization of the lung.

(b) *Chronic Interstitial Pneumonia*

(Non-Tuberculous)

(*Chronic Pneumonia, Cirrhosis of the Lung, Fibroid Phthisis*)

Chronic interstitial pneumonia is *a productive inflammation of the lung, characterized by the formation of fibrous tissue which is the product*

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of granulation tissue, causing induration and contraction of the organ. The process may be *peribronchial or interalveolar.*

A large number of these cases follow *chronic pleurisy and empyema* (pleurogenous pneumonia). The disease is therefore associated with dense adhesions which lead to *retracted and misshapen thoraces* with resulting *respiratory embarrassment* and further *secondary changes,* to *which I will again refer.*

Mediastinal growth, aneurism, abscess of the lung, peribronchitis, syphilis of the lung, hydatid disease and traumatism are among the causes of pulmonary fibrosis to be considered in making the prognosis.

(c) *The Pneumonokonioses*

(Zenker)

Pneumonokoniosis is an occupation disease in which there is fibrosis of the lung. The disease may be caused by the inhalation of dust, flour, or other noxious substances.

The inhalation of coal dust (*anthracosis*), steel dust (Zenker's *siderosis*), stone particles (*silicosis*), mineral dust (*chalicosis*) and cotton (*byssinosis*) are among the leading causes of fibroid proliferation in the lung.

In most of these cases the greater changes are in the apices of the lung where macroscopically there are abundant evidences of fibroid growth, misshaped and contracted lung, and collapse of large portions of the lung, while other changes are included which must be appreciated to justify safe prognosis.

General Conclusions

The prognosis of (a) chronic pneumonia following the acute lobar infection is often good. This is true of those cases in which the process is limited—the fibrosis does not extend—where there are no secondary heart changes, and after a reasonable time the lung learns to adapt itself to the slight abnormality which remains unchanged. *This forecast is applicable to chronic lobular pneumonia of limited extent.*

When the process is extensive, patients are made uncomfortable because of cough, respiratory insufficiency, consecutive heart changes, and resulting deformities. They may live during many years and die of intercurrent disease, but they are never well and their activities are limited unless perchance they are favorably influenced by climatic conditions. *Bronchiectasia, atelectasis, tuberculization, right heart insufficiency and stasis within the pulmonary, portal, and renal systems* (*ultimate dropsies*) are among the complications which influence prognosis.

The further consideration of the prognosis of (b) chronic (non-tuber-

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culous) interstitial pneumonia, and (c) the pneumonokonioses, justifies the following conclusions:

Unless the process is due to *specific deposit* (rare) there are no means at our command which influence existing fibroid changes.

Cases of *pleurogenous origin* may live during many years in comparative comfort without advance of the process; if the heart has accommodated itself to the changed conditions there are no threatening symptoms. These patients are easily fatigued and are often short of breath.

In all chronic cases the heart offers valuable prognostic data. The *right heart is naturally overtaxed by the obstruction in the pulmonary circuit* and with extensive fibrosis, dilates; this leads to hypertrophy with accentuation of the second pulmonic sound. *With advancing disease the dangers of myocardial insufficiency and degeneration are added.*

In the terminal stage, the patient's life is threatened by the resulting obstruction in the venous system, causing in turn cyanosis, liver and kidney changes, splenic hyperemia, ascites and edema.

The extent of the bronchiectasis and atelectasis in these cases is a powerful and unfavorable factor with failing heart strength.

The involvement of the bronchial glands (lymph nodes) is of great significance and *often lays the foundation for extension of tuberculosis.*

A surprisingly large number of chronic interstitial pneumonias including the pneumonokonioses develop tuberculosis.

We found in the *knife grinders* who worked over emery wheels, before the modern protective appliances were installed, that all developed *chronic interstitial pneumonia; that over 90 per cent of these who lived over ten years, showed positive evidences of pulmonary tuberculosis.* We have found the workers in an American knife factory who came from Sollingen, Germany, where they had previously worked and who had continued at their work more than five years, that, in spite of modern appliances, all of them showed evidences of siderosis; many of these have died of tuberculosis.

The chronic interstitial changes of the workers in coal mines and in an atmosphere of coal dust, as has been proved by experiences in America and on the continent, rarely become tuberculous. "All forms of chronic interstitial pneumonia may develop and die of tuberculosis" (Juergensen). Juergensen makes the following statement: "I hesitate to diagnose interstitial pneumonia and to exclude tuberculosis so long as there is normal physical strength and great mental activity, a quiet and strong heart."

The chronic pneumonia offers reduced resistance to acute infection, and many die of acute pneumonia.

Restitution to full health is impossible. The process due to the pneumoniokonioses is often stayed when not too far advanced. When the patient changes climate and his work, he may live many years.

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The prognosis is often influenced unfavorably by an intolerant stomach due to consecutive hyperemia.

Persistent evening rise of temperature, with accelerated pulse and loss of weight are unfavorable, and suggests tuberculosis or some other added infection.

Emphysema, when limited, is physiologic, when extensive it adds to the respiratory embarrassment and is unfavorable, increasing the work of the right heart.

With bronchiectatic cavities there may be absorption of septic and pyemic organisms, which reduce vitality and lead to serious *constitutional disturbances.*

Uncomplicated non-tuberculous cases have only rarely caused alarming hemoptysis in our experience. *Heredity* materially influences the incidences of the tuberculization of chronic pneumonics.

Children of tuberculous parents are handicapped.

The prognosis is more favorable in the adult than in children, so far as length of life is concerned.

Apex fibrosis is less favorable than is change at the base of the lungs.

Persisently rapid pulse, regardless of other symptoms is always ominous, and demands the most cautious search for its cause; *usually the complication of which it is an expression is serious.*

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4. Emphysema

(*Pulmonary Emphysema*)

Emphysema is a condition in which the air cells are abnormally dilated and the lung enlarged. *Surgical emphysema,* the escape of air into the pulmonary walls, following injury or surgical operation is not included in my consideration of this subject.

Vesicular or pulmonary emphysema may be either

(a) Compensatory
(b) Hypertrophic
(c) Atrophic.

(a) Compensatory emphysema

Compensatory emphysema develops when after collapse of lung tissue or extensive consolidation, unaffected portions of the lung assume increased function and fill the void. With atalectasis associated with bronchopneumonia, chronic pleurisy, adhesions, and with fibroid overgrowth—chronic interstitial pneumonia—large and chronic pleural effusion, pyopneumo-

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thorax and pneumothorax, compensatory lung changes including emphysema follow. The prognosis depends entirely upon the ability to influence the primary condition; once this is removed the lung accomodates itself, and function is practically normal. The discouraging feature is the inability to influence the underlying process. Each case naturally demands separate consideration (See separate sections).

(*b*) *Hypertrophic Emphysema*

Most forms of emphysema are of the mixed type; there is enlargement of the lung, the alveolar walls are dilated and the interstitial tissue is more or less atrophied. Emphysema is relatively frequent. Frankel found positive evidences of emphysema in 5 per cent of 911 post mortems. We found 4 per cent of 6,300 cases of internal disease. Emphysema is not a disease of early life, though children with chronic bronchitis or stenoses of the respiratory tract develop it. It is more frequent after the fortieth year and most frequent in those of advanced age.

Men develop emphysema oftener than women.

Heredity bears the same relation to emphysema as it does to asthma. James Jackson, Jr., found in Louis' wards 18 of 28 cases with positive heredity.

Emphysema, asthma and *chronic bronchitis* are usually associated conditions. *Bronchitis is the primary lesion in the majority of emphysemas. Bronchiectasia and emphysema* are frequently present together; in these cases there is preceding and persistent bronchitis also.

Fixed thorax is being more and more considered as a cause of emphysema and asthma (favorable for operation). *Emphysema is probably dependent upon inspiratory or expiratory stenosis or enfeebled respiratory strength.* Emphysema is often found in cases in which there is both inspiratory and expiratory obstruction.

Emphysema is aggravated by occuptions which require heavy work, lifting heavy loads, the playing of wind instruments or the inordinate use of the vocal organs (glass blowing, etc.). *When emphysema develops with chronic bronchitis* (*winter cough*) or any bronchial catarrh which continues unrelieved, it is progressive and is likely to lead to secondary circulatory changes.

Chronic bronchitis, "fixed thorax," and emphysema lead to aggravation of all subjective symptoms during cold and damp weather, also on exertion. *Cyanosis and marked dyspnea* are evidences of associated heart insufficiency, as a rule. *Asthma recurring at short intervals or unrelieved during long periods* increases existing emphysema and invites secondary changes. *The greater the respiratory weakness* (*muscular insufficiency of the respiratory muscles*) *and the more advanced the dilatation of the right ventricle, the less likely are the symptoms of emphysema to improve.*

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Persistent cough aggravates existing conditions, showing unrelieved bronchitis or secondary change. *Abnormally prolonged expiratory movement* is evidence of advanced emphysema in the presence of subjective symptoms. *Marked change in the shape of the thorax* (barrel-shaped thorax) is evidence of chronicity, and with the emphysema remains unchanged. *Marked change in the size of the heart,* particularly to the right, is present in advanced emphysema, and when associated with *myocardial insufficiency* is serious. In chronic and extensive cases the area of heart dullness is masked by the overlying dilated and enlarged lung.

Chronic nephritis, dilated heart, bronchitis and emphysema is a quartet of conditions at once serious, and while life may be prolonged, is fatal in the end.

Hypertrophy of the heart may prove sufficient during many years to carry some emphysematous patients along. In all of these suitable climatic and cautious treatment are important factors in prognosis. *Rapid pulse* with *increasing dyspnea* with or without increasing cough is always ominous. Arhythmia after long or short periods of emphysema is unfavorable and indicates degenerative change. Dropsies either limited or general are always unfavorable. *Dropsy is a terminal complication.*

Relative mitral and tricuspid insufficiency may develop after overtaxing the heart, or during acute exacerbation of existing bronchitis and asthma. With stimulation and rational treatment these threatening conditions often yield; they return on slight cause. *Myocardial degeneration is the usual cause of death.* Stasis unrelieved leads to liver changes, congested kidney with albuminuria, gastrointestinal disturbances and cerebral congestion.

Naturally the *extent of the existing bronchitis is paramount* in most cases, as is also *asthma* to which we have repeatedly referred.

Emphysematous patients who develop pneumonia (bronchopneumonia usually) offer an unfavorable prognosis.

I saw one case of fatal *pneumothorax* follow the *rupture of the apex of an emphysematous lung* in a post mortem made by Fischer (Frankfurt). In this case other dilatations were seen on the surface with thin walls like tissue paper. The apex was converted into cavities, several of which had ruptured.

Emphysema, without serious complication, even with asthma and bronchitis, may not shorten life; such patients may live many years and die of intercurrent disease. Many cases do not advance to involve larger parts of the lung or cause marked secondary heart changes. *Inherent weakness of the alveolar walls* (Virchow) invites progression. The two factors of greatest importance in the prognosis of emphysema are the behavior of the bronchial element and the ability to prevent disturbance of heart function with consecutive changes (stasis). *Cardiac insufficiency* once present, though it may yield to treatment, is certain to recur. Dyce

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Duckworth has reported fatal *hemoptysis* with emphysema, and Osler mentions "an old emphysematous patient . . . . . death followed the erosion of a main branch of the pulmonary artery by an ulcer near the bifurcation of the trachea."

(c) *Atrophic Emphysema*

I have considered cases in which there are atrophic changes in connection with the hypertrophic form of the disease, and there mentioned that most emphysemata were of the mixed type.

The *characteristic atrophic* form is found in old subjects in whom there is persistent respiratory embarrassment because of great dilatation of the air cells, the disappearance and atrophy of the alveolar walls and consecutive cavities. No treatment influences these cases.

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5. Gangrene of the Lung

Gangrene of the lung is always a *secondary infectious process* in which the death of either a circumscribed portion of the lung or diffuse areas takes place. Pulmonary gangrene is either embolic (metastatic) or bronchogenic. In my experience I never met but one case in which recovery followed the positive diagnosis of pulmonary gangrene—it was a sequel of an apex pneumonia in an adult aged 30 years. Lebert claims 6 recoveries in 36 cases; no other clinician has ever approached such encouraging results.

Pneumonia is the most frequent primary infection. Infections in which there are infectious emboli may cause the death of lung tissue. The clinical history of gangrene with the characteristic sputum and odor make its recognition relatively easy.

Pneumonia in diabetics invites pulmonary gangrene, which is promptly fatal (See Diabetes Mellitus).

Pneumonia with erysipelas or other streptococcus infections has supplied several cases in our series, all fatal. *Hemorrhagic infarct with septic conditions in nephritis* occasionally leads to pulmonary gangrene. The

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gangrene of pulmonary malignancy is one of the factors which increases the septic and typhoid condition and causes death.

Thrombosis or embolism of a branch of the pulmonary artery with septic conditions—typhoid, smallpox, pneumonia, or any other malignant infection—may cause gangrene. With all the prognosis is the same. Recovery is so rare as not to be expected.

Wilson Fox found one lung involved in 90 per cent of the cases investigated; the right in 54; the left in 36; the lesions were multiple and scattered in 22.5 per cent; limited to one lung in 77.5 per cent.

Laennec saw 2 cases in his entire practice. We have had 5 cases in 6,300 internal diseases. In over 37 years of active practice we do not recall 10 cases in private and hospital practice. 1.6 per cent is the proportion to other causes of death given by several observers (See West, S.). Multiple lesions are not uncommon with gangrene. Narther reports 8 cerebral abscesses in 49 autopsied cases of pulmonary gangrene—16 per cent.

Gangrene is exceedingly rare with pulmonary tuberculosis. Lung abscess and gangrene are occasionally coincident. Infection following pulmonary injury may lead to fatal gangrene. Our patients have usually died after from 5 to 14 days with symptoms of general sepsis and asthenia. In all cases the prognosis should be guardedly given; small abscesses with moderate necrobiosis may lead to recovery. In these cases, as in all who recover, a cavity remains from which there is more or less expectoration, often fetid, and in subacute or chronic cases there may be intermittent septic fever with final multiple foci and death after many weeks or months.

Hemoptysis—profuse bronchial hemorrhage—occasionally causes death.

Wherever possible, x-ray examination is indicated. With increased surgical technic the future may prove the prognosis of pulmonary gangrene to be more encouraging than it is at present.

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6. Abscess of the Lung

Lung abscess is a *surgical affection;* unless cured by nature's processes or surgery, it is always fatal. It offers only reasonable hope of

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recovery when superficial and surgically treated. To accomplish its relief by surgical means it must be favorably located, single and circumscribed. Multiple lung abscesses are almost always fatal. The outcome must depend upon the primary location and extent of the infection as well as the resistance of the patient, his age, and nature's ability in the absence of surgical intervention to wall off the disease. It may be secondary to pneumonia, pyemia, septicemia, injuries to the lung and chest wall, malignant growths, subphrenic abscess, liver abscess, and hydatid disease of the liver and lung. With pulmonary tuberculosis abscess of the lung often develops, also with pyopneumothorax which condition it may also cause.

There are a number of cases recorded which followed the aspiration of foreign bodies, also neck and thorax operations. With malignant growths of the lung or surrounding organs (esophagus) abscess may develop. The *pyemic abscesses* are of embolic origin and are usually multiple. *Perforation* of lung abscess may suddenly fill the air cells causing threatening or fatal asphyxia; *pyopneumothorax* follows pleural perforation and is always a serious complication.

In those cases which nature or the surgeon cures, there is gradual improvement of the general and local conditions; the sputum diminishes, the physical signs disappear very largely, and finally x-ray shows cicatricial contraction or a cavity walled off, or in other cases, a contracted cavity communicating with the bronchial tree.

The extent of lung abscess may be studied by means of the Röntgen ray, and valuable diagnostic and prognostic data are thus obtained.

7. Neoplasm of the Lung

New growths in the lung are either (a) primary or (b) secondary.

(a) Primary Neoplasms.—The primary neoplasms are exceedingly rare and these are usually carcinomatous, taking their origin in a bronchus, usually of considerable size (Aschoff). The occlusion of a large bronchus by the new growth leads to bronchiectasis. Primary cancer soon invades large portions of the lung, offers characteristic physical signs and x-ray picture. In some there is pleural infiltration and bloody effusion. Enlargement of supraclavicular, at times axillary, glands may be among the early secondary pathologic changes. The upper lobe is most likely to be the seat of primary carcinoma. *Pulmonary gangrene* may complicate primary carcinoma. Primary pulmonary cancer may originate in the epithelium of the air cells (rarely) or in the metaplastic bronchial epithelium (See Isaac Adler's splendid monograph for full data concerning the origin and growth of primary neoplasm of the lung). Aschoff claims that primary neoplasms of bronchial origin often originate in tuberculous cavities. In some of these cases the primary growth is small

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and gives rise to but few symptoms, while distant metastases offer the leading clinical data and cause death; thus, metastatic brain tumor may offer the only prominent symptoms. When the growth is *infiltrating* (a variety of primary lung cancer), large areas of lung tissue are involved.

I base my conclusions upon pathologic data which seem justified, and to these I add my unfortunate clinical experience with primary malignant growths of the lung. Adler, who has given this subject great thought and investigation, concluded one of his chapters as follows:

"Neglecting in this place all further detail, it may be briefly stated that it is at present the common consensus of opinion, and probably justly so, that the great majority of primary carcinomata of the lungs develop from the bronchi and that a cancer of the lung is, taken strictly, a bronchial carcinoma; that, on the other hand, a carcinoma starting from the lung tissue itself occurs, but is extremely rare, and is built up, not of flat, but of cylindrical epithelium."

The course of primary lung cancer may be either *rapidly fatal, acute* and *galloping*, or with symptoms of increasing pressure and *bronchopneumonic symptoms* the typical picture of lung cancer is presented; in some cases the features of *mediastinal compression* are in the ascendency, or the invasion of the *pleura* may materially influence symptoms and the course of the disease. In none of these clinical types is there hope of recovery. The x-ray examination offers hope of early diagnosis aided by the direct inspection of the bronchi, but unfortunately symptoms are not sufficiently pronounced early to lead either the physician or the patient to take advantage of these refinements of diagnosis.

(b) Secondary Lung Growths.—Secondary lung growths may follow primary cancer of distant or near organs. The breast and thyroid offer the primary seat of most metastases; they also follow stomach, pancreatic or genito-urinary growths. Secondary lung growths are usually multiple and infiltrate both lungs. With secondary lung growths, *cancer* or *sarcoma*, lymphatic involvement, bronchial, axillary, cervical or inguinal may develop. The pleural invasion or pressure leads to *hydrothorax*, usually bloody.

With cachexia, enormously emaciated, and with respiratory embarrassment, these patients die of exhaustion. Besides cancer and sarcoma, fibroma, lipoma, myoma, teratoma, and osteoma have been found in the lung (Aschoff).

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E. Diseases of the Pleura

1. Pleurisy

(*a*) *Fibrinous Pleurisy*

(*Dry Pleurisy, Pleuritis sicca*)

When dry pleurisy is of primary origin it usually follows in a previously healthy subject after cold or traumatism. Probably but few reach middle life without having at some time had limited pleurisy; in many the process of repair, after the plastic deposit on the pleural surface leads to agglutination of the visceral and parietal pleura, or adhesions, which may or may not give rise to symptoms. *Primary dry pleurisy* runs its course with but slight constitutional disturbance in from 2 to 7 days. In all of these cases the clinician must bear in mind the possibility of an underlying primary lesion (tuberculosis, pneumonia, etc.).

Associated Symptoms.—When pleurisy is *secondary* to *carcinoma, gangrene, traumatism* in which there is *fracture,* or *abscess,* the prognosis of the plastic pleurisy is of no importance; the primary disease offers the leading data.

Pleurisy with croupous pneumonia often adds to the discomfort and may, when severe, influence prognosis unfavorably though the toxemia and extent of the primary disease with the resistance of the patient remain the paramount factors.

(*b*) *Serofibrinous Pleurisy*

(*Pleurisy with Effusion*)

We consider the tuberculous pleurisies separately (see Tuberculous Pleurisy—Section on Tuberculosis). Many cases considered non-tuberculous during long periods finally prove to be tuberculous. Besides tuberculous infection serofibrinous pleurisy may depend upon the *pneumococcus, streptococcus, influenza bacillus, typhoid, diphtheria,* and a variety of other infections. The majority of *pneumococcus pleurisies are pleuropneumonic* and their prognosis depends upon the virulence of the lung inflammation and all other conditions which we have considered in connection with the prognosis of pneumococcemia (See Pneumococcemia).

Pneumococcus pleurisy often becomes *purulent* when it offers a good prognosis, early detected and radically treated (See Empyema). The *septic* or *streptococcic* or *staphylococcic pleurisies* must naturally depend upon the nature and malignancy of the infection as well as the extent of the pleural change, the amount of the fluid, the early recognition of its presence, and a variety of other data which we consider in connection

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with the symptoms and rational treatment. Most *influenzal infections* in which there is serous effusion are pleuro- or bronchopneumonic. The prognosis depends upon the same factors as are considered with the preceding clinical types.

Associated Symptoms.—With *typhoid fever, diphtheria, scarlet fever, polyarthritis* and *nephritis* the addition of pleural effusion is always a serious complication, more, because it is evidence of malignancy or severity of the primary disease.

Serofibrinous pleurisy associated with *abscess, bronchiectasis, gangrene, pericarditis, peritonitis, purpura* and *polyarthritis* is considered with these conditions in separate chapters.

Most pleurisies of childhood are of pneumococcus origin and offer a fair prognosis. The prognosis of serofibrinous pleurisy depends on the nature of the primary infection, the associated lesions in other organs, the height of the fever and tissue degeneration, the mechanical effect of the effusion, the effect of all upon the circulation, the early diagnosis and rational treatment.

High temperature persisting with effusion particularly after early aspiration, with or without repeated chill, leads to the suspicion of purulent change. The height of the temperature offers no clue to the nature of the infection. *Fall of temperature or decided remissions* before aspiration may in most cases be interpreted as indicating a mild course. *Slight temperature persisting after aspiration* is not unusual, neither is it unfavorable. In uncomplicated cases we have expected the temperature to fall to or near normal in seven days after aspiration. Persisting temperature after the seventh day with increase of fluid and good pulse is not unfavorable in the non-tuberculous cases. In cases which have been considered non-tuberculous, continued temperature, physical signs of fluid, rapid pulse, with or without night sweats, the chances favor an unrecognized tuberculosis. *Gastro-intestinal symptoms* are usually present and yield with the relief of the pleural pressure. *Cough* persisting is suggestive of unrelieved pressure, associated bronchitis, or lung involvement.

The *severity of pain* during the early hours does in some cases indicate the depth and extent of the pleurisy. This is not to be accepted without considering the possibility of exceptions. *Increase of urinary secretions*, at times *polyuria*, is favorable and denotes absorption of fluid unless there is proof to the contrary of its dependence on other factors.

Blood pressure in favorable cases is not materially changed from the normal. Decided fall is unfavorable. Emaciation is to be expected, but loss of flesh after radical treatment, failure to enter upon a satisfactory convalescence is indicative of associated complication, should lead to thorough investigation and suggests the possibility of tuberculous complication.

The *amount of effusion* is not an expression of the malignancy of the infection. There are cases of malignant infection in which the effusion

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is not large; on the other hand, the less malignant infection may be associated with large exudate. There is no rule.

Associated collapse of lung (atelectasis) with *weak heart* is unfavorable. *Grocco's triangle* is usually present with most fair sized effusions; it is of diagnostic, not of prognostic value. *Encapsuled effusion* may remain unrecognized longer than free fluid in the pleural cavity, and convalescence is therefore correspondingly retarded. The average favorable serofibrinous pleurisy runs its course to a favorable termination in from 3 to 4 weeks. The fever gradually falls, the heart strength increases, the physical signs improve, the *dullness or flatness does not disappear entirely either after aspiration or absorption*, but in the course of several months return of normal percussion note is to be expected.

The *return of the friction* sound after its original disappearance is favorable, for it indicates absorption or removal of fluid. In favorable cases the deformity of the thorax which follows from adhesions and neglect of proper treatment can be favorably influenced by pulmonary gymnastics and climatic change. The former alone, in primary non-tuberculous cases is sufficient.

Persistent dyspnea with or without weak myocardium in rationally treated cases is unfavorable and demands thorough search for its cause. In cases which promptly lead to adhesions and in which the lung is compressed and bound, unable to expand, there will be a long period before there is compensation. In these cases mechanical treatment (pulmonary gymnastics) often leads to brilliant results, but patience and perseverance are necessary.

The *unfavorable pleurisies* are those which have been neglected, in which the lung and other organs are misplaced, in which the heart is weak, the fever uncontrolled, the absorption slow, the improvement unsatisfactory after aspiration, and in which there is the picture of *sepsis*. In spite of these unfavorable features a number of these cases in which tuberculization does not follow, recover fully with more or less misshapen chests.

Delirium and other *evidences of involvement of the sensorium*, with rapid pulse and typhoid condition, are characteristic of the graver pleurisies. But few cases run an absolutely acute course.

General Considerations.—The sudden deaths reported by some are exceedingly rare. In our practice we never met but one sudden death from serofibrinous pleurisy. In that case the effusion had not been detected during many weeks; preparation was being made for aspiration during which the patient suddenly expired without preceding alarming heart weakness.

Double serofibrinous pleurisy is exceedingly rare: most of these cases are in reality *hydrothorax* dependent upon circulatory or other obstruction.

Interlobular pleurisy is more frequent than has been heretofore sup-

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posed. The diagnosis is easily made, as is that of all serofibrinous pleurisies by x-ray examination. *Interlobular pleurisy* (involving the surfaces between two lobes) may cause considerable malformation and troublesome adhesions, and unless the possibility of such encapsuled serofibrinous effusion is considered in the absence of the Röntgen rays the diagnosis will not be made. We refer to interlobular purulent pleurisy in the consideration of empyema. Fraenkel and Dietlen have done yeoman's service in this field by giving convincing clinical and pathologic data. The prognosis of interlobular pleurisy is favorable. The prognosis of serofibrinous pleurisy of early life (children) is not unfavorable.

Pleurisies limiting themselves to the diaphragm, the mediastinum and the pleuritic thickening and effusion of pleuropericarditis (polyserositis) are not primary, and their significance must be separately considered with the associated conditions (See Polyserositis). The differential diagnosis of the tuberculous and non-tuberculous pleuritides is enormously assisted by the *leukocytic blood count.* We have invariably found low white counts in our tuberculous cases and have prognosticated accordingly. The lymphocytes are relatively increased with tuberculous pleurisy as in other forms of tuberculosis. The average white count in non-tuberculous pleurisies is between 10,000 and 15,000.

Staehelin reports 13 deaths in 400 of serofibrinous pleurisy. In those previously depleted by disease (infection) with resistance lowered, the prognosis is correspondingly influenced. The influence of *early recognition* and *timely aspiration* on prognosis is paramouunt. *Complicating pulmonary embolism* and *thrombosis* are among the rare but fatal accidents.

Chronic interstitial pneumonia follows only those cases which lead to chronic pleurisy.

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(c) *Purulent Pleurisy*

(*Empyema—Pyothorax*)

The larger number of purulent pleural effusions are *secondary*, and most of these are found with the various types of pneumonia, either during the period of active inflammation of the lung or as a sequel following in the course of a few days or weeks.

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The more virulent types of empyema are those in which the bacterial invasion is greatest, in which the accumulation has remained unrecognized or neglected and time has been given for burrowing and distant infection, secondary pus accumulation in kidney, spleen, or other organs—occasionally purulent meningitis. The prognosis is also materially influenced by the previous condition of the patient, the character of the primary pneumonia, its extent and the behavior of the cardiovascular and renal organs, and the ability of the patient to resist disease.

Associated Symptoms.—*Either typical or atypical pneumonias* may have pus accumulation added. The more frequent are pneumococcus infections, but influenzal or streptococcus pneumonias are likely to suffer from this complication. In all, the prognosis is materially influenced by the added lesion but it may be positively concluded that in all, the early recognition of the pus, and its prompt removal, in the absence of associated depressing conditions, particularly if the primary disease has run its course, allows a reasonably good prognosis to be given.

Pneumococcus empyema offers a more favorable prognosis than do any of the other infections above mentioned.

Abscess of the lung associated with empyema offers a less favorable prognosis than does the latter alone. Yet in these cases in children and in adults during the active years of life, while the condition must be considered to be serious, the prognosis is not absolutely bad. I have the records of a number of cases of this kind in which, after a slow convalescence and long drainage, the patients have made a complete recovery, though with misshapen and sunken thoraces which finally improved under well regulated and long continued pulmonary gymnastics, in favorable surroundings.

Empyema with metastases, occasionally found with *puerperal fever, erysipelas, diphtheria, traumatism, tonsillitis, endocarditis, either benign or malignant infections of the walls of the thorax, or tuberculosis with or without pneumothorax,* offers a very grave prognosis. The prognosis is unfavorably influenced by a *rapid pulse* if this does not yield within a reasonable time to the radical treatment of the empyema.

Constitutional symptoms, such as *fever* and *delirium,* the former high and persistent, with or without chills, are found in the more malignant types of the disease; if they do not yield after rational treatment in a reasonable time argue against recovery.

Active delirium with rapid pulse and high fever in the *acute period of pneumonia with pyothorax* is suggestive of malignant infection and justifies an exceedingly grave prognosis.

General Statements.—*Spontaneous resorption* of pus from the pleural cavity is not likely to occur. *It certainly does not deserve to be considered* in the prognosis or treatment of the typical disease, and *he who depends upon it to the exclusion of radical methods of treatment is adding to the*

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dangers of his patient, reducing the chances of restoration to health, and is inviting rupture into lung or bronchus, deformity—usually irreparable —or death from exhaustion with general infection and possible amyloid changes.

Empyema necessitatis offers a poor prognosis for final complete functionating ability of the lung. Its ravages are often difficult of treatment, and may continue to prove a drag upon the patient during his entire life; they leave an avenue for future infection and almost continuous discomfort, besides the possibility of amyloid and other degenerations. In these as in all cases of empyema the great danger of pyemia and sepsis must be considered.

In *double empyema* of pneumococcus origin the prognosis is less favorable than with invasion of but one pleural cavity, but it is still good and the majority of these cases, promptly recognized and treated, recover. With the more malignant and far-reaching double empyemata of streptococcus origin the condition is graver; death usually follows, the duration depending upon associated conditions.

It is often surprising to note how promptly patients with empyema, with all appearances of serious illness, recover after the free evacuation of the pus.

The prognosis during *early life* is good in the large majority of cases. It is safe to place the recoveries above 90 per cent. Even during the first two or three years of life these figures are justified. In the *adult* during the active years of life, uncomplicated empyema offers an exceptionally good prognosis. Complications above mentioned must be considered. In *old age*, beginning with the fifty-fifth year of life, the prognosis is less favorable; fortunately the number of cases of empyema at this time of life is strikingly small.

The time of the complication is of great importance in prognosis. At the height of pneumonia of whatever bacterial type, the prognosis is less favorable than after the crisis. If in these cases there is cerebral invasion, if alcoholism, nephritis or arterial degeneration, or chronic metabolic fault (diabetes mellitus, gout, etc.), the prognosis is grave, and death follows promptly as a rule.

Recently Gerhardt, D., has described a type of empyema to which he refers as *parapneumonic empyema.* This condition is as a rule (I) associated with pneumonia at its height, (II) is of limited extent, (III) offers a favorable prognosis and (IV) the pus is remarkably free from microorganisms. The larger number of these cases will remain unrecognized, for the pus accumulation has been found so small and the added symptoms so few that it appears to the writer that its diagnosis is uncertain. Gerhardt claims however that in the Basel Clinic in 4½ years he recognized 20 cases of parapneumonic empyema in 300 cases of pneumonia, while in Wurzburg in 95 cases he found but 3 cases.

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If we accept the contentions of Gerhardt that such limited pus accumulations are frequently present with pneumonia, and adopt his characterization of the complication as *parapneumonic empyema*, we are justified in concluding that the condition does not materially influence the prognosis of the primary disease and that its own prognosis is good.

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(*d*) *Tuberculous Pleurisy*

See Tuberculosis (Section I).

(*e*) *Chronic Pleurisy*

There are cases of pleural effusion which persist during many months, which after the chest is emptied by aspiration return; they remain nonpurulent. Most of these in the end prove to be symptomatic and not true primary pleurisies. Some are tuberculous from the beginning and some of these may finally yield to time or radical surgical treatment; in others the fluid is finally absorbed; a number of cases are finally complicated by lung involvement and die of general tuberculosis. There are cases of a chronic character in which subjective symptoms and pleural thickening persist after pleuritis sicca. Such patients continue more or less out of health; they have some respiratory embarrassment, chronic cough, at times no cough at all—while pleuritic pains recur with the change of weather. All of these symptoms may follow any form of pleurisy including empyema, and are of no grave significance. Another class of cases is that in which pleurisy causes gradually increasing *proliferative changes*, resulting in thickening of the surfaces and extension to the interstitial tissue of the lung with *resulting fibroid pneumonia*, always chronic (See Chronic Interstitial Pneumonia). These cases primary pleural, may extend so slowly as to cause but few symptoms or little inconvenience during many years; the patients recognize their limitations and are worse during the winter and damp weather. Tuberculization is not uncommon.

Chronic pleurisy with multiple adhesions is frequently found post mortem without having caused symptoms during life. There are chronic pleuritides in which adhesions and proliferative lung changes lead to emphysema, bronchiectasis, and dilated heart. With increasing heart weakness dropsies may develop; also albuminuria and death results from exhaustion.

It not infrequently happens that pleural effusions are *encysted*, forming small or large *serofibrinous cysts*. The prognosis of these, when

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primary, is good. X-ray examination when possible should be used to determine the location and extent of these.

Hemorrhagic pleurisies are usually symptomatic of either carcinoma or sarcoma of the pleura or lung, malignant infection, hemorrhagic infarcts, terminal nephritis, tuberculosis or other grave primary lesions. These are therefore not true pleurisies. In all the prognosis is bad.

2. Hydrothorax

The transudation of non-inflammatory fluid in the pleural cavities is secondary, and purely symptomatic. It is usually an expression of circulatory insufficiency or compression and a part of general dropsy with myocardial insufficiency. Circulatory obstruction or insufficiency leading to hydrothorax may fill one or both pleural cavities. With heart lesions the hydrothorax is often unilateral; renal hydrothorax is almost always double.

Causes.—Carcinoma, grave constitutional anomalies, the graver anemias, Hodgkin's disease, pericardial adhesions and growths of the lung and pleura may by pressure cause hydrothorax. The prognosis of all these conditions is bad.

Associated Symptoms.—*With heart lesions* there may be material temporary improvement but hydrothorax is usually a terminal complication and when persistent during several weeks, without relief of the myocardial weakness, death is not long postponed. *Ascites and hydrothorax* are usually present at the same time.

3. Pneumothorax

(a) Hydropneumothorax
(b) Pyopneumothorax

Air in the pleural cavity is symptomatic. Pneumothorax is rarely present without either *serum* (a) hydropneumothorax, or *pus* (b) pyopneumothorax. Pneumothorax results when the pleural cavity is in communication with the external air; hence in the larger number of cases there is, either because of disease or trauma, perforation of the lung. In considering emphysema we call attention to the rupture of superficial emphysematous cavities; in our consideration of tuberculosis we also mention this accident. With whooping-cough, in rare cases, rupture of the lung may occur during a violent fit of coughing. Abscess and gangrene of the lung superficially located or burrowing, empyema rupturing into the lung, the breakdown of malignant nodule (carcinoma or actinomycosis or sarcoma) or perforation from the stomach through the diaphragm, perforation of the esophagus, aneurismal rupture, abscess of the liver, injuries to the

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chest wall, following the use of the aspirator needle, and in occasional cases rupture of the healthy lung during sleep or on only slight exertion, may all cause pneumothorax. We have recently received the history of a pneumothorax in an apparently healthy young man while playing billiards. These accidents do not always cause inflammatory changes (pleuritis) but, as a rule, they do. S. West believes that 90 per cent of all pneumothorax is secondary to the rupture of a tuberculous cavity or the breakdown of superficially located tubercle.

Statistics.—Osler mentions the "spontaneous development" in pleural exudates of the gas bacillus (B. aerogenes capsulatus, Welch). Emerson reports 48 cases of which 22 were tuberculous, 6 due to trauma, 10 of aspiration, 2 spontaneous, 2 with bronchiectasis, 2 abscess of the lung, 2 due to empyema, 1 gangrene of the lung, and 1 abscess of the liver.

Saussier's statistics show 62 per cent due to tuberculosis. Of 131 cases he found 29 due to empyema.

General Considerations.—The statistics of Walshe correspond with those of S. West. West, considering the possibility of rupturing a healthy lung "by any force which respiration can bring to bear upon it" concludes that it is possible, and cites pneumothorax resulting from whooping-cough and straining during labor. The direct results of pneumothorax are the collapse of the lung, and the displacement of organs. The danger from collapse of lung tissue which makes it useless is great, particularly when the breathing surface of the opposite lung is lowered by infiltrating disease. Besides the collapse of the lung on the side of the pneumothorax, the opposite lung suffers more or less from collapse, contains a reduced quantity of air, and "a smaller aerating surface on which the blood vessels are exposed to the air." With these conditions there is "embarrassment of the circulation which pneumothorax causes" (West). Because of these facts the greatest danger of pneumothorax immediately follows the perforation, within the first hour, and West contends that "the immediate prognosis improves with every hour that life is prolonged."

The ability to accommodate the lung function to the suddenly changed respiratory conditions, and the condition of the heart and the opposite lung, are important factors in framing the early prognosis. Naturally the prognosis is best when the lung has been previously normal. In cases of advanced tuberculosis the early symptoms may be largely cardiac and less pulmonary. Perforation leading to pneumothorax without advanced infiltration, or in the apparently healthy because of sudden change of respiratory conditions leads to greater respiratory embarrassment. In both, the ability of the heart to come to the rescue largely influences the prognosis. In some cases of tuberculosis where the process is not far advanced, pneumothorax without causing hydro- or pyothorax, may have a salutary effect, just as artificially produced pneumothorax in properly selected cases proves beneficial in a proportion of cases.

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Sudden cardiac insufficiency with collapse is the leading danger of pneumothorax. Pneumothorax is not of necessity a complication of the more advanced cases of tuberculosis; the rapidly advancing cases are most liable to perforation. Much depends upon the local change at the point of rupture; it may be extensive there, but limited elsewhere.

Persisting dyspnea is always significant of danger; with its relief and a fairly strong heart the immediate danger is decreased. It is possible for the perforation to seal itself and the air to absorb, if effusion is absent. Naturally the primary tuberculosis may be so far advanced as to prove the immediate cause of death.

Additional Statistics.—West in a series of 101 cases was positive of the duration in 39 and knew approximately in 37. Of the 39 cases, 10 patients died within the first 24 hours; "2 within 20 minutes and 30 minutes respectively of the attack; the other 8 within a few hours." "18 had died by the end of the first week, and 21 by the end of the fortnight; to which may be added 8 more cases, in which the duration cannot be quite determined, though it was certainly less than 14 days, making thus 29 out of 39 cases which were fatal within the fortnight, i. e., nearly 75 per cent. In other words, 3 out of every 4 cases." Six more died within the second fortnight. "Of the 35 cases in which the duration was uncertain, 9 were admitted with pneumothorax and died in the hospital; 10 developed pneumothorax in the hospital, and left at varying dates after the attack, some of whom were known to have died subsequently at their own homes; while 18 patients were admitted with pneumothorax and left with it. Of this second group, taking all the cases together, 10 died within the first month, 8 more within the second, and 2 more within the third—making 19 in all."

"Taking the two series together of 74 cases, 45 died within the month, i. e., 60 per cent; 9 more died within the second month, making 71 per cent." Seven were alive at the end of the third month, one at the end of the fifth, one at the end of the ninth. West reports 20 cases under his immediate care of which 12 died and 8 recovered—60 per cent mortality. The records of St. Bartholomew's Hospital for 14 years give the same mortality.

Special Considerations.—*Pneumothorax due to empyema*—rupture through the chest wall or into the lung with *empyema necessitatis*—offers a more favorable prognosis than does tuberculosis or other pneumothorax.

The clinician in offering prognosis must consider as suggested by West:

(1) "The immediate risk to life."
(2) "The possible duration of life."
(3) "The chances of ultimate recovery."

(1) *The Immediate Risk to Life.*—We have called attention to the greater danger immediately following the perforation. In deciding on

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the outcome, the dyspnea and circulatory obstruction, as shown by dyspnea, the condition of the opposite lung, the resistance of the patient and the underlying (primary) cause are the leading factors to be considered.

(2) *The Possible Duration of Life.*—The length of the patient's life depends largely on the extent and nature of the primary lesion, the heart condition, the resistance, the character of the effusion and the complications.

(3) *The Chances of Ultimate Recovery.*—We have seen recoveries in our series. We are watching a physician who almost two years ago after a number of years of latent tuberculosis (supposed cured) without warning, developed threatening pneumothorax. He is living, engaged in literary work, walks well and seems to be making a slow convalescence under favorable climatic conditions.

West places the average of recoveries at 10 per cent. The St. Bartholomew's statistics yield over 25 per cent. West's own statistics in "20 cases show 5 complete recoveries, in 3 the recoveries from pneumothorax were complete, but the patients died subsequently of phthisis; and in 3 others recovery was incomplete. Besides these, I have seen one other case in consultation in which recovery was complete and the patient remained well for many years."

Without effusion the prognosis is always more favorable. Purulent effusion (pyopneumothorax) offers the most unfavorable prognosis. X-ray examination will prove of great assistance in showing the extent of the primary deposits and the amount of effusion and displacement.

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4. Mediastinal Diseases

Because of the relative importance of the organs within and in close relation to the mediastinum, the fact that most mediastinal lesions lead to pressure, the *prognosis of all mediastinal lesions is grave.*

The leading mediastinal tumors are: *sarcoma*—these may arise from lymphatic glands, the thymus or cellular tissue (Woodwark, Aschoff and Mueller), *secondary cancer, lymphadenoma* (glandular), *dermoid and hydatid cysts.*

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Associated Symptoms.—The *pressure symptoms* and *physical signs* with all of these conditions are positive, as they are also with aneurism, specific lymphadenitis, abscess and emphysema following injury or perforation of surrounding organs. *Tuberculous glands* may lead to suppuration and pressure. Hare made an exhaustive study of the diseases of the mediastinum, including 520 cases. He found 134 cancers, 98 of sarcoma, 21 lymphoma, 7 fibroma, 11 dermoid cysts, 8 hydatid cysts; lipoma, gumma and enchondroma. Sarcoma is oftener primary than cancer.

The prognosis of mediastinal growths is absolutely bad. With increasing dyspnea, cyanosis, edema and heart insufficiency these patients often die after weeks of wretchedness.

The x-ray pictures make it possible to watch the growth, locate it and recognize the changed relations of the included and surrounding organs (Rieder, Holzknecht). *Mediastinal abscess* may perforate; it has been the cause of death with erysipelas or it may develop without known cause. *Mediastinitis which is suppurative is always a serious disease.* Recovery from abscess may be expected in about one-half the cases. Hare says 40 per cent. Acute *thymus death* has been separately considered. Pressure from an enlarged thymus gland, if great, impinges on the mediastinum with fatal result, if not relieved at once. We have seen several cases in which death followed a few days of suddenly increasing mediastinal pressure with Hodgkins' disease and lymphatic leukemia.

The *heart changes materially influence prognosis with all mediastinal displacement;* usually the displacement is to the left. *Venous stasis* is common and in cases which are terminal, the engorgement of the face and arms, one or both, with dyspnea and deep cyanosis tell of the approaching end. Tumors which press on the trachea and esophagus show their progression by increasing stridor and dysphagia. *Hydrothorax* and *palpable nodules, enlarged supraclavicular glands all aid diagnosis and prognosis. Cachexia* is often extreme with mediastinal malignancy. According to Mueller, Fr., death follows in about one year in the average case. The course of the disease depends upon the nature and rapidity of the growth.

Blood counts particularly *leukocytic counts* will often prove of value in differentiating thyroid, thymus enlargement and malignant growths. With thyroid or thymus pressure there are the blood changes mentioned in our separate consideration of disease of the ductless glands. The increased lymphocytosis (30 to 50 per cent) with these is of great diagnostic and prognostic value (See Thyroid and Thymus Disease).

Displacement of the mediastinum due to *pleural* or *pericardial effusion* may prove fatal unless promptly relieved. Hare includes 6 cases of *hematoma* in his series of 520 cases of mediastinal disease. Most hematoma of the mediastinum are of traumatic origin and are exceedingly grave. The extent can be decided by x-ray examination, but the subjective symptoms will offer the best guide for the forecast. If dyspnea and cyanosis

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are relieved or improving, if the pulse is correspondingly better there is hope of ultimate relief unless there are associated unfavorable conditions.

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Section III

Diseases of the Circulatory Apparatus

A. Arteriosclerosis

(*Arteriocapillary Fibrosis, Atherosclerosis, Atheromatous Degeneration, Endarteritis chronica deformans, Endarteritis chronica nodosa, Arterial Degeneration*)

Arteriosclerosis is a progressive nutritional disturbance of the arterial wall, with swelling, thickening and sclerosis of the intima primarily, increase and degeneration of cellular elements, partial necrosis and calcification, either diffuse or nodular, in which all coats are finally involved; the media more particularly when the arteries of the extremities are affected. There is in advanced cases, change of a productive character in the adventitia (peri-arteritis). This definition of Marchand is almost universally adopted by clinicians and pathologists and at once demonstrates the possibility of either limited degeneration, or what is more frequently found—almost universal invasion of the arterial tree with consecutive changes in many organs. The correct conception of the causes and nature of the pathologic processes included in arterial degeneration proves the complex character of the lesions in the individual case, that the prognostic and clinical problems are among the most complicated and obscure in the whole field of internal medicine, and that the *dictum of Bruce* finds profitable application in connection with our study of this disorganizing process, in which he holds: "The best prognostic use to make of symptoms and signs is indirect; not to value them individually, but to diagnose by them the cause and nature of the pathologic process, and then to frame our forecast by these."

Arteriosclerosis furnishes the fundamental morbid processes in the larger number of deaths after the fortieth year. Arteriosclerosis of the heart, kidney and brain is the cause of 22 per cent of all deaths after the fortieth year of life.

Advanced arteriosclerosis is synonymous with old age. Whenever

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present, the changes are suggestive, for we find the skin altered and wrinkled, the parenchymatous organs and muscles atrophied, the bones show trophic changes and fracture easily and the mental status is below par.

The pressure in the aorta and peripheral vessels in the aged is not necessarily the same, it is higher in the ascending aorta and in consequence is lower in the periphery.

The increase of cardiovascular disease during the past two decades has been recognized by all clinicians. This increase is greater the farther we are separated from hospital practice.

Of 5,708 cases of internal disease seen in our private practice during the past seven years of which we have full records, there were 623 *cases of marked and advanced arteriosclerosis* 10.8 per cent, 101 *cases of angina pectoris*, 1.77 per cent, and 110 cases of chronic interstitial nephritis, 1.9 per cent.

The change is appreciated when we quote from a long-hand written report of the lectures of Benjamin Rush delivered over 125 years ago, in which that experienced and busy clinician makes the statement that he had seen but "one case of angina pectoris" and mentions the name of another Philadelphia physician who had also seen but one case.

The gravity of arterial degeneration is shown further by the increase of other heart lesions directly dependent upon the same process. Thus in an analysis of our cases, *we find* 4.2 *per cent* showing evidences of degenerative endocarditis; (in contradistinction to inflammatory) 4.7 *per cent of aortic obstructive and degenerative lesions of the aorta, and* 8.6 *per cent of myocardial degenerations.*

The study of our material justifies the conclusion that hurry, worry and excesses are at the bottom of the majority of our cases; the stress of modern life, syphilis, and the enormous influence of heredity are among the leading factors with which we must reckon.

In all cases there is a *period of hypertension,* either recognized or unrecognized which precedes the fully developed symptoms which are directly due to arteriosclerosis—to this we will again refer.

There is a physiological hyperplasia of the intima during early life.

For purposes of diagnosis and prognosis we consider the separate artery as an organ, a part of the body which has positive functions to perform; its task is not single but multiple; the performance of its daily undisturbed work is attended even during the earliest years of life with a compensatory deposit for the preservation of these organs and the continuity of the circulation. As soon as this physiological hyperplastic change of the intima because of age, overwork, strain, toxemia, or from any other cause is forced into a stage of hypertrophy, we have the beginning of arteriosclerosis.

The leading factors which influence prognosis are the following:

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1. Age

Arteriosclerosis is present more or less advanced in most subjects who have lived beyond the fiftieth year. If the arterial tree is subjected to critical microscopic examination this fact is fully established.

Arteriosclerosis may persist for years without giving rise to a single symptom, without in any way interfering with the comfort of the individual; it is well borne when it is associated with the tolerance and compensation that are expected in the subject advanced in life. These favorable conditions do not prevail during early life.

Young subjects do not bear arteriosclerosis well; in these, evident and palpable lesions are not long present without marked evidences of progression and the development of organic lesions in vital organs, unless the process is promptly controlled by proper treatment. If of *syphilitic origin* and not far advanced the artery may and often does yield to intensive treatment.

No person is too young or too old to be thoroughly searched for arterial change; the prognosis so far as tolerance and length of life are concerned is unfavorable in the younger subjects.

Romberg in 774 *male patients*, excluding all juvenile arteriosclerosis at the Marburg Klinik found arteriosclerosis:

Between the 20th and 29th year in 4.89 per cent.
Between the 30th and 39th year in 14.28 per cent.
Between the 40th and 49th year in 29.67 per cent.
Between the 50th and 60th year in 41.55 per cent.
Between the 60th and 69th year in 57.77 per cent.

Among 703 *females:*

Between the 30th and 39th year in 0.78 per cent.
Between the 40th and 49th year in 6.1 per cent.
Between the 50th and 59th year in 34.25 per cent.
Between the 60th and 69th year in 52.00 per cent.

Severe arteriosclerosis in young subjects involving the aorta and other vessels are not uncommon. Andral, Fischl and Chiari, found in all subjects examined in Prague between 2 and 25 years of age 48.7 per cent with beginning evidences of arteriosclerosis in the intima of the aorta.

When arteriosclerosis is the prime cause of death, it is likely to claim its victims during the productive years when they ought still to be able to continue their occupations; as Bruce has said "when work ought to be still carried on in the interest of the family and country, at an age when a man's reasonable ambitions, as a rule, have not been attained." Grassman offers the following data which corroborate our conclusions: Of 151,083 who died in Germany 13,247 had cardiovascular lesions, including cases of cerebral apoplexy. From 15 to 30 years he found diseases of the

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circulatory organs the cause of death in 7 per cent; between 30 and 60 years 14.5 per cent of all deaths were due to the same causes. In Bavaria in 1907, 17,000 died of diseases of the cardiovascular system and 7,000 of cancer, thus two groups were responsible for 25 per cent of all deaths.

2. *Heredity*

The influence of family history on the prognosis of arteriosclerosis is paramount. In subjects burdened with the family history of arteriosclerosis there is progression of the degeneration on slight cause.

Histories in which one or both parents and several of their children have died of *coronary disease* are not uncommon; neither are the instances of *cerebral hemorrhage* in many members of a family at almost the same age unusual.

The appreciation of the influence of heredity on prognosis, interpreted by the physician and the patient, may if heeded, lead to rational cautious living and appropriate occupation, which will often postpone unfortunate tendencies and thus prolong life.

3. *Syphilis*

We have elsewhere considered the influence of specific infection on the arterial tree (See Syphilis of Arteries) and will also consider *aneurismal dilatations* which are often of specific origin, separately.

It is a fact that arteriosclerosis (*arteritis specifica*), of syphilitic origin when early recognized is amenable to treatment and may yield after severe and threatening subjective symptoms.

4. *Worry and Stress*

The arteriosclerosis which follows long continued worry and stress, particularly with unfavorable family history, is likely to advance insidiously, to involve vital organs (heart and kidney), before subjective symptoms are sufficient to bring the patient to the physician. The obstruction in the arterial tree is shown by persistent hypertension and hypertrophy of the left ventricle, all of which make the prognosis grave. It is surprising, however, to note how in individual cases, if the patient is removed to a favorable environment, where rest, relaxation with freedom from care and rational living obtain, he improves, and how his life may be prolonged. With the baneful factors continuing, such lives are promptly ended, usually with evidences of added *myocarditis* and *chronic interstitial nephritis*. (See Occupation in this chapter.)

5. *Alcohol*

Alcohol is directly and indirectly a factor of the greatest importance in the causation and prognosis of arteriosclerosis. Alcoholics are as a rule

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careless of their health, some are *inordinate eaters*, some have *perverted appetites*, others to tempt their appetites use *deleterious condiments* (pepper, etc.); they eat at irregular hours; while alcohol itself may not produce hypertension and arterial change, the productive changes wrought in liver, heart, brain and kidney, with the factors above mentioned lead indirectly to arteriosclerosis and the inclusion of the changes in the vital organs which lower the resistance of these subjects and lead to death. The contention of Richard Cabot that alcohol does not cause arteriosclerosis based on the examination of the arteries of alcoholic inebriates has not been generally accepted by the profession; as we have intimated we know that a large number of alcoholics die of cardiovascular disease, particularly arteriosclerotic processes and must accept that fact as proved in framing a forecast. Harlow Brooks' report of 400 autopsies and the clinical evidences obtainable are sufficient to establish the influence of alcohol on arterial disease.

The following is the table compiled from Brooks' statistics:

Artery.	Cases.	Etiological Factors.
.....	400	Alcohol, 149; among laborers, 115; nephritis, 51; syphilis, 38; old age, 38. Males, 275; females, 125.
Aorta.....	301	
Visceral trunks.....	368	
Coronary arteries.....	270	Alcohol, 107; nephritis, 35; syphilis, 27; excessive tobacco, 9.
Brain.....	132	Alcohol, 48; nephritis, 21; syphilis, 19.
Renal.....	81	Alcohol, 43; nephritis, 10; syphilis, 10.
Pancreas.....	74	Alcohol, 19; syphilis, 9; senility, 9.
Hepatic.....	43	Alcohol, 12; nephritis, 8; syphilis, 6; senility, 3.
Splenic.....	35	Alcohol, 9; syphilis, 7; nephritis, 4; endocarditis, 2; senility, 2; tuberculosis, 2.
Lungs.....	...	Alcohol, 4; syphilis, 5; senility, 5; tuberculosis, 4; nephritis, 2.
Celiac axis.....	19	Most of them with alcoholism. Sclerosis of mesenteric, all cases with adiposis.
Spinal vessels.....	20	Alcohol, 4; syphilis, 4; most of the rest in primary spinal diseases.

Alcoholic parents beget children who are likely to develop arteriosclerosis early in life.

6. *Lead*

Lead poisoning leads to *hypertension, arterial thickening, chronic nephritis* and when advanced offers an unfavorable prognosis for *Restitutio ad integrum*. When detected early, and the patient is removed from the atmosphere of lead, the prognosis is not unfavorable, though the arteries remain permanently altered.

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7. *Tobacco*

Lauder Brunton says of the influence of nicotin, "The rise of blood pressure is so great that I have never seen it equaled after the injection of any drug, with the exception of suprarenal extract. The rise is due to contraction of the arteries. The ultimate effect is to increase the rapidity of the heart." I am fully satisfied that in many cases tobacco is among the cause of arteriosclerosis, that it aggravates existing hypertension and arterial degeneration, that unless used in moderation it is injurious to adults and that for growing boys it is "distinctly harmful."

The use of tobacco in the presence of hypertension and arteriosclerosis acts unfavorably on the organic process.

8. *Infection*

The influence of infection in causing hypertension and arterial change has been noticed and studied by most clinicians. Thayer and Brush examined 4,000 consecutive cases admitted to the Johns Hopkins Hospital and found changed arteries in the percentages noted of the patients under fifty years of age who had been the subjects of the following factors:

After scarlet fever, radials palpable in	16.4	per cent.
No causal factors with palpable radials in	16.5	" "
Pneumonia, radials palpable	17.0	" "
Diphtheria, radials palpable	17.0	" "
Malaria, radials palpable	20.0	" "
Typhoid fever, radials palpable	26.0	" "
Rheumatism, radials palpable	34.0	" "
Alcoholics, radials palpable	46.8	" "
Hard work, radials palpable	57.5	" "

Added infection of any kind in subjects with pronounced arteriosclerosis is always serious and adds enormously to the danger. Pneumonia is almost uniformly fatal in the presence of advanced arteriosclerosis, while *typhoid fever, sepsis, rheumatism, and erysipelas* also offer unfavorable prognoses.

With some acute infections in the presence of arteriosclerosis the pulse may continue slow, full and reasurring during the first forty-eight hours (particularly with pneumonia), but soon there is a break, the blood pressure falls and the heart becomes insufficient.

9. *Occupation*

Occupation is of paramount importance in the etiology and prognosis of arteriosclerosis.

Arteriosclerosis is the result of long continued wear and tear, more

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tear, "which is the result of abuse," than wear which as Weir Mitchell said is "the result of use."

The busy brain worker, the man of enormous responsibilities, the worker who with his worries is obliged to hurry, whose rest is insufficient, who is wearing his bearings and holding the string taut, is gradually but certainly encouraging arterial degeneration, he may work during months or even years with hypertension, no warning has led him to relax until he has run to a fall and is beyond the stage of hypertension and has fully developed arteriosclerosis. This is the history of hypertension and arterial degeneration as it is found among professional men, including physicians, lawyers, bankers, brokers, engineers, all occupations which tax the brain and are sedentary. In physicians, the tendency is toward coronary disease. With but one notable exception all members of the Vienna faculty who have died within the past two decades have yielded to coronary sclerosis and myocardial degeneration. In our own country the number of physicians who are claimed by coronary disease or general arteriosclerosis is surprisingly large.

Romberg says "Everyone acquires his arteriosclerosis within the circuit which he has taxed most."

There is no more interesting question in connection with the etiology and prognosis of arteriosclerosis than nervous stress. It "winds up the best brains in the community" (Bruce). The combination of "intellectual stress and emotional stress" which characterizes the "strenuous life" is at the bottom of physiological collapse.

The early appreciation of the effect of occupation with appropriate treatment during the period of hypertension often does much to relieve the tension and prevent progression to organic change. In these cases the timely detection of a *trace of albumin* and an *occasional hyalin cast* is a warning which if recognized may prove life saving.

The truth of Romberg's dictum is proved by the location of the greater changes in the arteries in the different occupations.

The brain, heart and kidney vessels show greatest changes in those of sedentary habits—i. e., in *brain workers.* In *workingmen,* the arteries of the extremities are most involved. In the *wives of farmers* the arteries of the legs are the seat of degeneration; among *wealthy females* we often find the mesenterics involved, often the coronaries, sometimes both.

In all, when arteriosclerosis develops rapidly after an unrecognized period of hypertension there is likely to be kidney invasion; this is true of those cases in which there is enormous accentuation of the second pulmonic sound, in which the pulse continues tense, and there are evidences of hypertrophy of the left ventricle. Some of these apparently subacute cases may lead to death within a few months.

In the majority, an early appreciation of the effect of occupation on prognosis by the individual, with prudent and cautious self-control, the

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ability to bring appetite to reason, the practice of sobriety, temperance and abstinence, much can be accomplished to prevent the onward march of the degeneration. Benjamin Franklin's aphorism is applicable, "Against diseases known, the strongest fence is the defensive virtue, abstinence."

10. Overeating

The arteriosclerotic who cannot control his appetite, is unable to control the process which threatens his life. Overeating invites and produces degeneration; it increases it because it throws an extra burden on the heart, vessels and digestive organs. It interferes with metabolism and chokes the furnace to the disadvantage of the cardiovascular system as well as most organs within the domain of the splanchnic and renal vessels.

A single error of diet has often ended life which might have continued in comfort during many years. This is particularly true of coronary sclerosis and myocardial degeneration. These are the deaths which are incorrectly attributed to "*Acute indigestion*" which are increasing with noticeable frequency.

11. Mechanical Factors

Mechanical factors have a decided influence on prognosis, the sclerosed artery has been robbed of its elasticity, it is lengthened and abnormally tortuous, it demands auxiliary force (*vis a tergo*) which in the end may prove insufficient. The ability of the heart muscle to continue to compensate for the lack of assistance normally offered by artery and muscle, to which it has been accustomed, naturally influences the prognosis enormously.

Mechanical strain aggravates existing sclerosis and may lead to *rupture* and *sudden death* or to *aneurism*.

12. Chemical and Toxic Factors

Chemical and toxic factors unquestionably exert a baneful influence. These may be provocative of hypertension, or when present the continuous poisoning increases the ravages of the process in all directions. The retention of wornout material, the results of faulty metabolism, persistent hyperglycemia (*Diabetes mellitus*), the blood surcharged with uric acid and its products, with gout, the other toxic states which are associated with faulty secretion and excretion, the influence of the ductless glands, particularly the adrenals in throwing their secretions into the blood-stream, are all factors which need to be considered in framing the prognosis of the individual case.

The "*Metabolic group*" is important, for in these cases there is malnutrition, the tissues are poisoned by the products of malassimilation and as Bruce has well said "they are starved at the same time."

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Diabetics usually show evidences of marked arteriosclerosis, the disease is rarely hypotensive, usually there is a normal or elevated blood pressure and often the pancreatic arteries are markedly changed. (See Diabetes mellitus.) *Gout* shows cardiovascular changes in almost 50 per cent of cases.

13. Hypertension

There is a considerable period of hypertension which precedes profound changes of an organic nature in the arterial tree, which however, in the majority of cases is not recognized, because of a natural tolerance; and the almost immediate compensation.

If hypertension persists unrelieved, and the factors which continue it remain uncontrolled, organic changes in vital organs are usually present, particularly in the heart, kidneys and within the splanchnic area, before the patient presents subjective manifestations.

Hypertension long continued is the leading cause of arterial degeneration.

Prognosis of hypertension depends entirely upon the time of its recognition, in no other way than by early recognition can its influence on heart, peripheral vessels, kidney and brain be controlled.

When arteriosclerosis is established, hypertension is not a necessary feature; our statistics elsewhere given in this chapter prove that arteriosclerosis may show normal, subnormal or high blood pressure. (See Blood Pressure Study.) "As a raised blood pressure is itself productive of degenerative changes in the vessels, we have good grounds for believing that if the rise be detected early, and counteracted by proper regimen and treatment, the vascular changes which it would otherwise produce might be prevented, and life very considerably prolonged. The earlier this is done the better, and I think it is only likely to be done by the sphygmomanometer being used as frequently by the physician as the stethoscope or thermometer are at present." (Lauder Brunton.)

The prognosis is good when with hypertension there are no evidences of associated lesions.

Hypertension in young subjects with uniformly thickened arteries, smooth and tense, who appear prematurely old, demands a guarded prognosis; it is usually progressive.

Hypertension with marked renal symptoms, often without albumin, *"non-albuminuric nephritis"* is no longer uncomplicated, but in such subjects the degeneration of the arteries has commenced and the prognosis must be made accordingly; these are amenable to treatment. While the organic changes cannot be overcome or influenced unless specific, the prognosis so far as life is concerned is not necessarily bad.

It may be safely concluded that *uninfluenced hypertension* in most cases is associated with changes in the renal vessels, the process is partly glomerular and partly includes the lesions of the granular kidney.

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14. Kidney Invasion

With advanced arteriosclerosis there are, as a rule, marked changes in the kidney substance; the evidences of nephritis are positive. Pathologists and clinicians in the study of arteriosclerosis have during the past sixty years made repeated attempts to satisfactorily explain the sequence of invasion of the heart, arteries and kidney and their reciprocal relations without reaching conclusions which may be accepted as final. The clinician knows that there are cases in which the process in the kidney seems to be primary and the arterial and heart changes secondary, on the other hand, there are cases in which the clinical history proves the presence of arteriosclerosis and heart compensation before there are positive evidences of interstitial or mixed nephritis. Post mortem investigation shows the invasion of the kidney in the overwhelming number of cases of advanced arterial degeneration.

The recent investigations of Fischer, J., who examined 550 cases of marked hypertension in which the clinical and pathological evidences of nephritis were carefully noted are interesting: 62 per cent of these showed positive evidences of nephritis; 15 per cent were suspicious; 23 per cent gave normal urines. Excluding cases with blood pressure below 160 mm. Hg. in only 3.6 per cent was the urine normal. Autopsies of 42 cases showed positive nephritis; in 14 of these the urine during life showed no evidences of kidney disease. Krehl from his material reports in patients with a blood pressure of 200 mm. Hg. or higher 87.4 *per cent with nephritis*—of these he *autopsied* 43 *cases, of which* 42 *gave positive evidences of nephritis.*

Adami says "arteriorenal problems are among the most complicated and obscure in the whole of pathology."

In presenting this subject we feel the safest conclusion to reach is that arteriosclerosis and hypertension may occur without the symptoms of renal invasion, that with high blood pressure, tense thick arteries, hypertrophy of the left ventricle, there is nephritis in almost all cases. The absence of albumin and casts from the urine during long periods with such positive objective features does not argue against the presence of nephritis and the prognosis should be accordingly made.

With arteriosclerosis in any of its stages the prognosis is unfavorable in proportion to the extent of kidney involvement.

15. Coronary, Myocardial, Endocardial and other Heart Lesions

In all cases of arteriosclerosis in which there have been evidences of coronary disease the prognosis for *Restitutio ad integrum* is bad, though life may be prolonged, and the patient may die of intercurrent disease years after the initial symptom of angina pectoris or anginoid disease.

The coronary trunks may be atheromatous, tracing them into their

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intramuscular network, the finer branches may be free from any trace of disease and thus sufficient blood is sent to the myocardium to maintain the left ventricle. Such cases, unless overtaxed, may live many years with but few symptoms. Patients may have a single severe attack of angina pectoris or suffer repeated "small attacks," symptoms may be present which prove deep involvement of the coronaries and yet the heart pang and other reminders of coronorary sclerosis may be absent for months or years at a time; and it is not at all unusual, particularly in thoroughly treated specific cases, or in cases which have developed murmurs and slight dilatation to find the symptom complex permanently relieved. We refer the reader for the full consideration of the prognosis of coronary disease to the chapter on *Angina Pectoris.*

Myocardial degeneration associated with arteriosclerosis is always ominous; this is especially true of the senile heart, when overtaxed. The prevention of *mechanical strain* often makes it possible for these patients to live comfortably during many years; life may be sacrificed by a single indiscretion.

Arteriosclerosis of specific origin leading to myocarditis may yield to treatment.

With long continued hypertension and an overworked heart, there is great danger of sudden revolt of the heart muscle with disastrous results. With necrotic processes in the myocardium resulting from coronary occlusion, the prognosis is bad. Coronary disease is the most frequent cause of disorganizing changes in the myocardium. The closure of one branch of the coronary does not always lead to death. Such advanced disease is always serious.

The condition of the heart muscle is the most important factor in the prognosis of arteriosclerosis, in the myocardium rests the key of the heart and upon it we must depend.

In our experience myocardium degeneration accompanied one-sixth of all cases of arteriosclerosis at the time of its detection. The prognosis of myocardial degeneration is fully considered in another chapter (*Myocarditis*).

Advanced arteriosclerosis is associated with compensatory hypertrophy of the left ventricle. So long as these changes are sufficient, in the absence of added complications, the prognosis for life is good. Such subjects may live for years without inconvenience unless they overtax their cardiovascular system. We cannot subscribe to the dictum which holds that such hearts prove as resistant as normal hearts. They are not, they do not brook insult, they revolt on slight cause.

With advanced coronary sclerosis there is reduced heart strength and dilatation may lead to sudden death.

Long continued hypertension with hypertrophy of the heart is associated with nephritis in most instances and offers a bad prognosis.

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The condition of the peripheral arteries and the kidney are important factors to be considered in connection with the heart anomalies of arteriosclerosis.

Marked accentuation of the aortic second sound is proof of increased peripheral resistance and with aortic obstruction (vascular), showing itself in a well marked basic systolic murmur, we may be sure of advanced sclerosis, usually including the ascending aorta; conditions which are permanent but with favorable environment and right living the patient may live during many years.

Naturally *aneurismal dilatation* of the aorta alters the prognosis.

With marked *widening of the ascending aorta* and a corroborative x-ray picture, we have often found an area of tympany and exaggerated breathing to the right of the sternal edge in the aortic space and around it and the aortic impulse increased; this is of serious moment. Usually these cases are associated with coronary disease. (See Aneurism of the larger arteries.)

The *frequency of the pulse* with persistent high blood pressure is of prognostic significance. *Rapid pulse*, whether intermittent or arhythmic, with myocardial or other heart lesions, with or without high blood pressure tires the heart and reduces the chances of prolonging life. Intermission, arhythmia and irregularity, may persist during years without shortening the life of the patient. Such anomalies are well borne in older subjects; in the young in whom they arise suddenly, life is at once threatened. The prognosis is always better in those cases in which the heart has gradually fallen into the habit of being erratic and the muscle has learned to accommodate itself. None of the hearts with the above mentioned anomalies are dependable, though they may serve when undisturbed by added complications during surprisingly long periods.

Cardiac asthenia and pulmonary edema due to cardiovascular degeneration are usually terminal conditions and of grave import. Even these threatening complications may with proper care be followed by long periods of comparative comfort.

The *endocardial changes* of arteriosclerosis are degenerative and not inflammatory. The greater the invasion of the aortic cusps and the adjacent endocardium the worse is the prognosis. Simple aortic obstruction without incompetence due to roughness of the valves and the ascending aorta may persist during years without causing damage or symptoms when uncomplicated.

When the *aortic cusps* are so malformed as to become insufficient, a different picture is presented; the heart has an added burden, its further hypertrophy follows, the pulse amplitude shows the enormous load which such hearts are carrying and degenerative myocarditis, apoplexy, uremia or other complications must be expected. Such hearts are ready to surrender on slight cause.

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Increase of *physical signs* particularly in arteriosclerotics with diabetes and gout, fresh murmurs (*aortic*) with evidence of insufficiency is always ominous and shortens life. With *aortitis and diabetes* the prognosis is bad; there is always danger of *coma.*

Gangrene when an evidence of endarteritis obliterans is not a limited process, there are often associated metabolic faults (*diabetes, gout*), the arterial tree is extensively involved and prognosis as a rule is bad. Life has been prolonged in some cases by surgical interference but the extension is not usually long.

16. Vascular Crisis

(*Spasm*)

"Vascular crisis" is a term which was introduced very largely as the result of the investigations of Pel to characterize recurring, suddenly arising symptoms of a painful character in the domain of changed arteries.

Vascular crises are associated with diseased arteries in which the definite symptom-complex is due to vascular contraction, temporary narrowing of the artery; occasionally extreme dilatation or vasodilator paralysis may predominate.

Vascular spasm or crisis explain the sensory symptoms included in anginous attacks, intermittent claudication, some cases of Adams-Stokes phenomenon, evanescent muscular pains and cramps in the subjects of arteriosclerosis, abdominal angina, or the Dyspragia intestinalis intermittens of Ortner; the *crisis of tabes* in cases associated with arterial degeneration, a condition which is often present early in young tabetics and many cerebral and spinal symptoms of short duration.

Vascular crises are provoked by factors which throw an extra tax upon the heart and the organ invaded. This is a fact of enormous importance to be considered in prognosis and treatment.

Vascular spasm is evidence of developed arteriosclerosis, and is not present, in our experience during the early stage of hypertension; it always adds to existing dangers; more when vital organs (*heart and brain*) are involved.

The *anginous attacks* we have considered elsewhere; most of these are due to coronary spasm.

Intermittent Claudication

(*Dysbasia intermittens angiosclerotica*)

Vascular spasm of the lower extremities usually provoked by walking or movement of the limbs to which Erb called attention, and which

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is increasing with the increase of arterial degeneration may recur during long periods, may be associated with erythromelalgia, *Raynaud's Disease,* or may in cases of advanced obliterating endarteritis precede gangrene during long or short periods. *Erythromelalgia* as we have demonstrated (Elsner) is usually due to arteriosclerosis. Its symptomatology includes the *"red neuralgia"* of *Weir Mitchell,* but contrary to his original contention it may ultimately lead to sufficient obstruction of the circulation to cause gangrene or limited necrobiosis. (See Erythromelalgia.)

Acroparesthesia and many of the other sensory disturbances of the extremities are due to arteriosclerosis and associated vascular spasm. (See Acroparesthesia.)

Threatening brain symptoms—*vertigo, transitory paralyses, aphasia, also paraplegia and temporary abeyance of function in other organs* are often warnings of approaching danger due to vascular spasm.

Transitory blindness in one eye in the subject of arteriosclerosis may be dependent upon vascular spasm. In this connection the experience of Wegenmann is corroborative. Wegenmann's patient was a man aged sixty-three years who had arteriosclerosis and who had transitory periods of blindness in his right eye. On one occasion Wegenmann was present when the patient became suddenly blind. An ophthalmoscopic examination was made; the arteries during the period of blindness were found empty. They were converted into threadlike shining strands, yellow in color. Normal pulsation had ceased. The veins resembled threadlike but red strings. Pressure on the eye did not cause pulsation. This condition continued during ten minutes, the observer found as the spasm was relieved, the arteries filled and the veins dilated, with a return of pulsation and of sight.

It is a question whether the pains of *lead colic,* in which we know there is arterial change (hypertension) are not due to vascular spasm.

The prognosis of arterial spasm is not encouraging—an expression of fully developed arteriosclerosis—*it is a symptom of a far-reaching process.*

When vascular spasm causes the Adams-Stokes phenomenon because of arterial change in the vascular supply of the intraventricular septum, a condition which is not unusual, the prognosis of non-specific cases is absolutely bad. With specific arteritis it may cause sudden death.

Vascular spasm of the cerebral and spinal vessels has in some of our cases persisted during a number of years; finally these patients invariably succumbed to the underlying conditions.

Unless vascular spasm is dependent upon a removable cause such as syphilitic end-arteritis there may be improvement and temporary relief but never cure.

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17. Cerebral, Spinal and Peripheral Changes

The influence of *cerebral, spinal and peripheral changes* of the nervous system and psychoses are separately considered. *Neurasthenic conditions are common and rebellious.* (See Neurasthenia.)

18. The Blood Pressure Study of Arteriosclerosis (after the stage of hypertension)

The revelations of the sphygmomanometer (*blood-pressure study*) are too often misinterpreted to the disadvantage of the patient; this is particularly true of blood pressure in connection with arteriosclerosis. The suggestion to the patient that he "has blood pressure" is often depressing and starts an autosuggestion which may prove injurious.

With increased blood pressure sufficient to "meet physiological demands" the various tissues of the body are given a sufficient blood supply. Occasionally a high blood pressure causes weakness of the diseased walls of the vessel and rupture results, "a high blood pressure with this exception is not to be regarded as something evil, but as an attempt on the part of the body to keep our various organs working at their physiological optimum" (Fisher). *Elevated or changed blood pressure* is therefore often a conservative and compensatory process to be left undisturbed; at times encouraged; it is a balancing and protective measure.

Blood pressure study alone offers much less information of value in framing prognosis than is generally supposed.

Arteriosclerosis may be far advanced without marked change in the systolic pressure, it may remain normal; in some cases there is, after the initial period of hypertension persistence of the same pressure, while in another class of cases there may even be hypotension.

In the cases of advanced arteriosclerosis mentioned in the beginning of this chapter in connection with the study of 5,708 cases of internal disease I found persisting hypertension (above 180 mm. Hg.) in 181 cases or 3.17 per cent and striking hypotension in 21 cases. In 623 arteriosclerotics the per cent of hypertension cases was 29. Sawada found of 206 cases of arteriosclerosis, 122 not complicated with marked lesions, 12.3 per cent with high blood pressure. In 75 with heart complication and albuminuria 30.6 per cent showed hypertension. Janeway found 11.9 per cent of all of his cases of internal disease (7,872 patients) with systolic blood pressure above 165 mm. Hg. and 458 of these had permanent hypertension. Of 870 patients with hypertension at some time 62.4 per cent were men and 37.6 per cent were women. Of the 458 cases of persisting hypertension 67 per cent were men and 33 per cent women. Janeway found at the end of the nine year period the number of men dead were 6.2 per cent more than living; women living

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were 35 per cent more than dead. Thus 20.6 per cent more men died than women. This experience is confirmed by all observers—*women bear arteriosclerosis better than men, unquestionably the prognosis would be the same if both sexes were exposed to the same conditions.*

Arteriosclerotics bear operations badly, this is particularly true of men with high blood pressure who subject themselves to prostatectomy. A number of these develop uremic symptoms with suppression of urine within 24 to 48 hours of the operation fall into coma and die.

It will be seen from the statistics of Janeway and those which I offer, that *arteriosclerosis is not necessarily a hypertensive disease.* My figures differ because Janeway included all cases above 165 and I only those above 180 mm. Hg.

Blood pressure study calls attention to possibilities and should be so interpreted.

Young subjects who appear prematurely old with persistingly high blood pressure offer unfavorable prognoses.

High pressure with renal changes, also cases of "non-albuminuric nephritis" and dilated heart or associated coronary disease offer unfavorable prognoses.

Pulse Pressure

The study of the *minimum or diastolic pressure* which gives also the pulse pressure (difference between the systolic and diastolic pressure) is more important for prognostic purposes than the systolic pressure alone. It makes clear "the burden" which the heart is bearing. "Pulse pressure measures the energy of the heart in systole in excess of the diastolic pressure" (Stone).

A sustained diastolic pressure of from 100-110 signifies hypertension; it measures peripheral resistance and is therefore a "better index of hypertension than the systolic pressure" and "is less influenced by physiologic factors than the systolic pressure" (Stone).

In cases in which the blood pressure is high, but the normal ratio between the maximum and minimum (systolic and diastolic) pressure is not markedly altered, we are justified in offering a favorable prognosis for the chances are against grave organic change in favor of a stage of hypercontractility of the walls of the vessels, which rational treatment may relieve.

Sudden reduction of high pressure may lead to serious conditions, *including anuria, coma, myocardial weakness and death.*

Low systolic blood pressure after a period of hypertension with nephritis usually leads to sudden death because of "cardiac defect" (Allbutt).

The greatest differences in systolic and diastolic pressure, hence the highest pulse amplitude or pulse pressure, are found with advanced aortic disease (insufficiency), chronic interstitial nephritis with double

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aortic murmurs and marked cardiac hypertrophy. All offer grave prognoses.

Invasion of the splanchnics (the *mesenteric arteries*) is associated with high pressure during long periods and *with persisting toxemia usually due to intestinal disturbance throws added work on the cardiovascular system, influencing prognosis unfavorably unless promptly relieved.*

The great difficulty which we face in the problem of arteriosclerosis and blood pressure study is that we do not know the strength of the arterial wall; with normal or increased pressure miliary aneurisms of the cerebral arteries or ulcerating defects of the larger vessels may lead to hemorrhage (rupture); dilatations and various other irreparable complications.

With changed blood pressure, *cerebral warnings, including vertigo, spasm or convulsions, lapses of memory, active or passive cerebral hyperemia, associated edema, sudden dyspnea, increase of kidney symptoms including uremic poisoning or indiscretions may be followed by a decided break leading to death.*

19. Thrombosis

Arteriosclerosis is a frequent cause of thrombosis; the complication is always serious. With coronary disease suddenly developing thrombosis is a frequent cause of death.

With *sclerosis of the pulmonary artery*, multiple organized and firmly attached thrombi are not infrequently found post mortem which must have antedated death during comparatively long periods; the patients dying of other causes. *Arteriosclerosis of the pulmonary artery* may exist without change in the arteries of the body; *it is often found with mitral lesions and emphysema;* in such cases there is *increased blood pressure in the pulmonary circuit and hypertrophy of the right ventricle.*

Thrombi are more frequent in the smaller arteries and consecutive changes due to occlusion must be expected.

Thrombi in the aorta are frequent and may start emboli to the brain or other vital organs. *Hemorrhagic infarct secondary to aortitis with thrombosis in the brain, spleen, kidney or liver may lead to death. The thrombus of aortic aneurism is not so firmly attached as is the organized plug in the pulmonary artery.*

20. Ocular Changes

Advanced arteriosclerosis particularly when associated with interstitial nephritis shows evidences of change in the retinal vessels. The presence of *retinitis albuminuria* with arteriosclerosis never justifies any other than an unfavorable prognosis. Such patients stand on the edge

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of a precipice and may fall at any moment. They rarely live two years after the onset of the retinitis. *Cerebral apoplexy, uremia, pneumonia and sudden myocardial failure* are the causes of death.

Large and suddenly arising retinal hemorrhages are evidences of the terminal stage or far advanced disease.

Advanced arteriosclerosis shows involvement of the retinal vessels in the majority of cases. The ophthalmoscope therefore is a valuable prognostic aid.

21. X-ray

The revelations of the Röntgen picture in individual cases will prove of value in prognosis. This is particularly true of changes in the aorta (aneurism, etc.), and in the differentiation of specific and non-specific arteritis.

Our views concerning the prognosis of arteriosclerosis have been materially changed during the past fifty years. This fact is proved by the following quotations from Bamberger, who represented the climax of medicine in Germany sixty years ago, and from Romberg, who stands today as the exponent of all that is advanced in cardiovascular pathology and diagnosis. Bamberger said, "Atheromatous processes cannot be cured, hence they cannot be treated." Romberg holds: "While we are not able to alter the anatomic changes in the blood vessels, the seat of arteriosclerosis, we can nevertheless improve the functions of the organs invaded and exert material influence on the advance of the process."

The prognosis in every case of arteriosclerosis must be based not only on the subjective and objective manifestations which are evident, but a thorough inquiry into the patient's entire history, the influence of his occupation and his habits, the diseases which he has had, his "constitutional strength and physical training and disposition in earlier years, and more remote than these, his inheritance." (Bruce.)

In no other process does inheritance, the character of the individual, his disposition, temperament and circumstances play such an important rôle.

In arteriosclerosis there is often a single and preventable cause, not an extension of the degeneration which produces the death of the patient.

Much naturally depends on the location of lesions; limited arteriosclerosis—a small plaque at the mouth of a coronary vessel—a small miliary aneurism of a cerebral vessel, circumscribed sclerosis with localized myocardial degeneration and rupture, may cause sudden death, while with disseminated change in the arterial tree, the patient may live for years in comfort, oblivious of his lesions.

"The first requisite for longevity must clearly be the inherent or inborn quality of endurance; of steady, persistent nutritive force, which

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includes reparatory force and resistance of disturbing effects; and a good proportion or balance between the several organs. The second requisite is freedom from exposure to the various casualties, indiscretions, and other causes of disease to which illness and early death are so much due." (Humphry.)

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B. Aneurism

Aneurism may be defined as a chronic dilatation of a blood vessel with productive (connective tissue) change of its wall, the cavity always communicating with the lumen of the artery. For our purpose we consider only the *circumscribed and diffuse dilatations.* The most common form of the former is the *saccular* aneurism, of the diffuse—the *spindle shaped.*

Miliary aneurisms will be considered in connection with cerebral apoplexy.

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Dissecting aneurisms are due to incomplete rents in the walls of a blood vessel; the layers of the vessel are undermined by the blood and consecutive deposit. This variety is of interest pathologically only.

The leading pathogenic factors to be considered in the formation of aneurismal dilatations are *diseased blood vessels, arteritis—usually specific arteriosclerosis; besides syphilis, typhoid fever, diphtheria, endocarditis (malignant) and other infections, traumatism and increased blood pressure.*

In our hospital and consultation practice we have found at least 90 per cent of all cases due to syphilis. Malmsten found 80 per cent syphilitic. *Recent experiences give positive Wassermann reactions with almost all aneurisms, particularly the aortic dilatations.*

Unquestionably syphilis leads to arteritis and arteriosclerosis in young subjects and thus lays the foundation for dilatation on slight cause.

The prognosis of all aneurismal dilatation so far as life is concerned depends upon its location, its size, the condition of the arterial wall, the blood pressure, the strength and condition of the myocardium and valves, the extent of degeneration of the arterial tree, the relation of the growth to the surrounding organs, the amount of pressure it exerts, the extent of paralysis (particularly of the vagus), the amount of pressure upon nerve trunks and bone tissue, the protecting influence of coagulation and thrombosis within the sac, the results and amount of obstruction to the blood stream which follows, as well as many other factors, including lesions in vital organs, brain, liver and kidney, which are likely to be associated with cardiovascular disease. More than two-thirds of all aneurisms are found in men between the 38th and 60th year. Cominotti found aneurism five times as often in men than in women. He found 24 between the ages of 24 and 40 years, 29 between 40 and 50, 18 between 50 and 60.

Marchand in 28 autopsies of aneurisms found 20 men and 8 women, 2 were between 30 and 39 years of age, 6 between 40 and 49 years, 10 between 50 and 59 years, 4 between 60 and 69 years and 6 between 70 and 90 years.

The greater frequency of aneurism in England and in the United States than on the Continent of Europe is established by statistical study. The negro is more disposed to aneurism than is the white man. Myers found in 320 deaths of soldiers in the English Army resulting from cardiovascular lesions 138 aneurisms; of 1,346 invalided soldiers 35 had aneurisms. Crisp reports 551 aneurisms, spindel and saculated, located as follows:

Aorta (thoracic)	175
Popliteal artery	137
Femoral artery	66
Abdominal aorta	59
Carotid artery	25

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Subclavian artery	23
Innominate artery	20
Axillary artery	18
Iliac artery	11
Arteries of the internal organs	8
Cerebral arteries	7
Pulmonary artery	2

Cominotti found in 181 aneurisms, 37 of the ascending aorta, 49 of the arch of the aorta, 29 of the descending aorta and 16 of the abdominal aorta.

Nature may either protect the arterial wall or occasionally, by its reparative process, cause obliteration of the sac and relative cure. Thus dense and organized coagula in moderate sized dilatations, without marked interference with heart or distant organs, may exist during years, and death may be due to other causes. *By the reinforcing of the aneurism with fibrous tissue the growth may become stationary. The tendency of all aneurismal dilatations is towards progression, with compression and adhesion to the surrounding organs. Rupture of the wall is the most frequent cause of sudden death.*

Thrombosis may prove sufficiently extensive to close the aneurismal sac and present a smooth surface to the blood stream.

Moderate dilatations may be smoothed and protected during long periods by dense and firmly organized thrombi.

A small artery with aneurismal dilatation may be side-tracked by Nature's processes without interfering with the heart or the general health. (Collateral Circulation.) (Jores.)

Infectious processes, tuberculosis particularly, may cause ulcerative changes in the arterial wall leading to aneurismal dilatation. This method of producing aneurisms holds only for the smaller arteries.

The *mycotic-embolic aneurisms* which arise during the course of malignant or infectious endocarditis are usually multiple and follow ulcerative changes in the walls of arteries. This is a part of a process which is always fatal.

Embolic detachments from aneurismal walls are not frequent; occasionally they may lead to sudden death, hemorrhagic infarcts in the lung, spleen, kidney, brain or other organs; rarely to gangrene.

X-ray examination of all aneurisms gives positive data which make clear the location, the size, the relations to surrounding organs, as well as other important facts which bear upon the diagnosis and prognosis in individual cases.

The further complications which influence prognosis are considered in connection with the separate aneurisms.

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1. Aneurism of the Ascending Portion of the Arch of the Aorta

Aneurism of the ascending portion of the arch of the aorta is a sequel of syphilitic aortitis, and is always fatal.

When the x-ray shows the presence of the dilatation, the radial pulses are unequal, there are other evidences of pressure with secondary heart changes, death may be expected at any time.

With aneurism of the aorta in any of its parts and associated coronary disease the patient's life is in constant jeopardy; such a patient is "always dying."

The thickness of the aneurismal wall and the size of the aperture communicating with the aorta influence the force of the pulsation ("expansile thrill"). The growth increases by expansion.

Thin aneurismal dilatations just above the aortic valve or of one of the cusps of the valve may rupture into the pericardium without having caused previous symptoms (Aneurism of a Sinus of Valsalva). With these cases coronary invasion and aortic insufficiency is not uncommon, the latter at times leads to hypertrophy of the left ventricle.

Dyspnea and cyanosis are not long endured, they indicate a tired heart and pressure with pulmonary obstruction.

Edema of the upper extremities—one or both—when once established is likely to persist until death.

Pulmonary edema on slight cause, particularly during and after coitus, is often a terminal symptom.

All pressure symptoms, once established are likely to continue.

The extent of compression showing itself in symptoms, is a valuable guide for prognosis and justifies conclusions which the experienced can usually reach concerning the average time which the patient may live—barring sudden rupture which is always to be expected with all aortic aneurisms.

2. Aneurism of the Transverse Portion of the Arch of the Aorta

The anatomic location of the arch leads to symptoms of compression often before dilatation is far advanced. Aneurism of the arch of the aorta is likely to be associated with some change of the ascending portion also, as the process advances.

The *displacement of the heart*, usually to the left, may exist without marked hypertrophy of the ventricle. *When the aortic valve is insufficient*, as often happens, *the hypertrophy is enormous.*

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Marked systolic bruit and *tracheal tugging are evidences of advanced aneurism.*

Paralysis of the left recurrent laryngeal nerve is proof of advanced aneurismal dilatation in the presence of other physical signs and persists unrelieved to the end. If the innominate is involved, or if there is sufficient pressure, the right recurrent may also suffer; under these conditions the end will not be long postponed in the average case.

The papillary changes are due to involvement of the sympathetic system and are proof of advanced disease.

3. Aneurism of the Descending Portion of the Arch of the Aorta

Aneurism of the descending portion of the aortic arch may exist during a considerable period without causing symptoms. The recognition is often postponed because of the failure to interpret the significance of the multiple symptoms of many intrathoracic lesions which are included when subjective complaints are made, and the further failure to take advantage of *Röntgen examination.*

The aneurism may cause *intercostal pain* during a long period when finally positive evidences of compression in *erosion of the dorsal vertebrae* (usually third to the sixth) is added; there may be evidences of bronchial and lung pressure, or the mass may present externally in the scapular region. *Rupture* into the pleura, bronchus or lung is the fate of a large number of aneurisms of the descending portion of the arch.

Early recognition of aortic aneurism wherever located which is possible by x-ray examination with immediate rational treatment, including the indicated rest, offers the only encouragement for the prolongation of life.

4. Aneurism of the Descending Thoracic and Abdominal Aorta

Aneurism of the descending aorta below the arch, may cause but few symptoms until advanced, when pains—intercostal and lumbar—with epigastric or thoracic pulsation persist. The *stomach and liver* may be displaced. *With abdominal aneurism the systolic bruit can be distinctly heard posteriorly, a symptom of great diagnostic and prognostic value in doubtful cases.*

Erosion of bone (vertebrae) *and other symptoms of compression, edema of the extremities are present in advanced cases.*

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5. Aneurisms of the Celiac Axis

Aneurisms of the celiac axis or its branches may prove of anatomic interest, they may not be diagnosticated *intra vitam* as there may be no symptoms. In one case I found the symptoms of hemorrhagic pancreatitis arise suddenly in a man age 65. The autopsy showed rupture of the disorganized axis into the pancreas.

The prognosis of splenic, hepatic and renal aneurism is equally bad. There may be *aneurismal dilatation of one of the mesenteric arteries, usually the superior*, which causes vague symptoms, may lead to death from rupture or it may be accidentally discovered at autopsy.

6. Aneurism of the Coronary Artery

Aneurism of the coronary arteries is exceedingly rare, leads to death by rupture into the pericardium or heart muscle. (Wardrop.) Griffith has collected these cases in a splendid article.

7. Aneurism of the Pulmonary Artery

Aneurism of the pulmonary artery or its branches is also rare. Our experience includes one case in which we failed to make the correct diagnosis (though aneurism was strongly suspected) because the aneurismal dilatation rested on the heart wall anteriorly and consequently did not show in the skiagram. Death resulted from rupture into the pericardium.

8. Aneurism of the Subclavian Artery

With *subclavian aneurism* we have seen long periods during which there was no advance of growth or symptoms.

The growth of an aneurism is rarely continuous; there seem to be sudden exacerbation in many. The hope of prolonging life rests in the strengthening of the arterial wall and the organization of coagula (thrombosis) by Nature's processes.

Landraf reports a case of aortic aneurism in which paralysis of the recurrent laryngeal disappeared. This is exceedingly rare.

The dissecting aneurism usually leads to early perforation; other aneurismal dilatations perforate in the later stages, after long periods of compression and expansion. *Fifteen to twenty per cent of all aneurisms perforate.* The perforation usually leads to prompt death; in exceptional cases a rent may be closed by a thrombus or perforation may

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take place into organized tissue, into a vein or into the substance of a solid organ when death may be postponed for a short time. *Location of an aneurism does not change the prognosis so far as its influence on life is concerned; with all, the outlook is equally grave, all stand on the edge of a precipice; when the fall is to follow no clinician can prophesy.*

We may safely conclude that aneurism is rarely cured by any method of treatment. *Nature's methods of spontaneous relief* we have already considered.

Death is the fate of most patients with aneurism within from six to eighteen months after the diagnosis has been fully established. There are exceptions to this rule; cases are recorded by all experienced clinicians which lived during years, but these are notable exceptions.

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C. Diseases of the Pericardium

1. Acute Pericarditis*

Acute pericarditis is a secondary inflammation of the pericardial sac, rarely primary, associated in the order of frequency with *rheumatism, tuberculosis, pneumonia, pleurisy, scarlet fever* and *typhoid fever.* It may also occur with other *exanthemata* as *measles, smallpox,* etc., and is not an infrequent accompaniment of *septic* and *pyemic infection.* It is in many cases coincident with *valvular lesions—endocarditis* and *myocarditis.*

Echinococcus disease and *actinomycosis* may provoke it; it is occasionally found with *gonorrhea,* may follow extension of cancer and sarcoma from the surrounding organs, may be secondary to perforation of the esophagus or of the pleura with empyema; abscess of the liver and subphrenic abscess may perforate into the pericardium as may pyopneumo-

* The reader is also referred to chapters on the separate infections where the prognostic significance of pericarditis is considered among the complications.

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thorax; gastric and intestinal ulcers with adhesions and inflammation may lead to pericarditis.

Chronic interstitial nephritis is often associated with pericarditis. Romberg quotes Frerichs and Rosenstein as having found the sac inflamed in 13 of 292 and 8 of 114 cases respectively—5.1 per cent.

Pericarditis may also complicate *scorbutus,* other *purpuric conditions, leukemia* and *pernicious anemia.*

Penetrating wounds of the thorax, gunshot wounds, erysipelatous inflammation of the thoracic walls or phlegmonous infiltration with suppuration when they involve the heart sac usually cause *purulent pericarditis* as do also the malignant perforating diseases already mentioned; all offer unfavorable prognoses.

The so-called *idiopathic pericarditis of children is almost always of tuberculous origin* in the absence of positive proof of other causes. (Rheumatism, scarlet fever, etc.).

When pericarditis accompanies puerperal sepsis it is likely to be purulent and fatal.

Naturally pericarditis is found in those of all ages since it is an accompaniment of so many infections, as well as other constitutional anomalies and accidents.

The pericarditis of rheumatism is present in from 5 to 6 per cent of fully developed cases in adults and from 10 to 20 per cent in children. In the majority of these *endocarditis with some change in the myocardium* is present. There are occasional severe cases in which the heart sac is involved before there are evidences of arthritis. A large number of *fatal cases of chorea* with and without joint symptoms and tonsillitides are at times complicated by pericarditis and are of rheumatic origin.

The prognostic significance of pericarditis depends almost entirely on the nature and gravity of the primary disorder. *The reader will find the subject separately and fully treated in connection with the consideration of the complications of rheumatism, tuberculosis, pneumonia, scarlet fever, pleurisy, typhoid fever, erysipelas, chorea, tonsillitis and all other infections, beside septic and pyemic conditions,* to which he is referred.

When pericarditis does not advance beyond the first or dry stage (*pericarditis sicca*) it has, *per se,* very little influence on the course of primary disease.

Romberg, however, reports 85 cases of pericarditis with 24 deaths, a high mortality. At Johns Hopkins Hospital Hoffman's statistics show among 7,770 medical cases admitted (1902-1911) 1,317 (1,044 males, 273 females) cases of circulatory diseases, among these were 22 diseases of the pericardium (14 males with 5 deaths—35.7 per cent) (8 females—2 deaths—25 per cent), of these 11 males had pericarditis with 3 deaths, 27.3 per cent, and 6 females with 1 death, 16.7 per cent.

The effusion may be *fibrinous, serofibrinous, purulent or blood stained.*

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The less severe types are fibrinous and serofibrinous with rheumatism; purulent effusion is associated with septic and pyemic infections and is always serious, usually fatal.

Those purulent effusions are most serious which are associated with puerperal sepsis, pyemia, malignant endocarditis and in cases in which there are bands of adhesion which bind the heart anteriorly when the pus is held in the dependent portion of the pericardium beyond the easy reach of the operator.

The blood stained effusion is usually found with tuberculosis, cancer, sarcoma, purpura or scorbutus. It is always an indication of serious constitutional disturbance and is likely to end in death.

The serofibrinous effusions with the infections (rheumatism, scarlet fever, tonsillitis) are, unless the primary disease leads to death, absorbed in the course of a limited period with resulting temporary or permanent adhesions.

The extent of the adhesions and their permanency are important factors in limiting the action of the heart and are considered in connection with *adherent pericardium.*

Moderate adhesions with partial obliteration of the heart sac do not often lead to permanent subjective symptoms after recovery.

Calcareous Pericarditis.—In a few cases there may be calcareous deposits in the pericardium, the prognostic significance of these depends entirely upon the extent of the degeneration, the condition of the heart muscle and the nature of the accompanying chronic changes in other organs. *Purulent pericarditis may be followed by calcareous deposit;* this is exceedingly rare as most purulent cases die.

Acute Myocarditis.—Acute myocarditis may be complicated by pericarditis. In these cases the spread is from the myocardium and invades the pericardium in the neighborhood of the primary muscle change.

But few cases of pericarditis are without more or less myocarditis. The extent of the latter is of paramount importance.

Myocardial inflammation associated with *pericarditis* when far reaching or in a previously weakened or diseased heart may lead to cardiac insufficiency. *Dilatation of the heart* is not infrequent; usually the right heart is involved, with relative muscular weakness. If in such cases the patient lives and there are adhesions or lowered vitality, myocardial degeneration may follow and there may be cellular infiltration, fibroid change or atrophy.

The heart and surrounding organs are tolerant of pericardial effusion during long periods. The sac may contain a large quantity of fluid without threatening life.

Rapidly increasing exudate is more threatening to life than is the gradual accumulation.

X-Ray Examination.—The assistance received from the Röntgen

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picture is not always to be relied upon in the presence of moderate effusion; it will nevertheless prove a valuable aid in prognosis in many cases. *Pericardial adhesions* are often beautifully clear in the picture, more particularly the *extrapericardial bands.*

Displacement of the lung with *tracheal pressure and involvement of the mediastinum,* often with *paralysis of the recurrent laryngeal nerve,* may prove serious and unless relieved becomes life-threatening.

Pulmonary edema with insufficiency of the right heart and dilatation of the ventricle may lead to sudden death.

When pressure leads to dropsy and there is associated myocarditis the prognosis is grave.

Thrombosis, either pulmonary or in the left innominate, increases obstruction and is usually fatal.

Pericarditis with chronic Bright's disease is a terminal complication (See Nephritis).

Symptoms referable to the nervous system as delirium, coma, convulsions, marked *apathy* and prolonged *insomnia* are evidences of the graver infections. With *osteomyelitis,* pericarditis adds a large element of danger to an infection already malignant.

The *behavior of the temperature* offers but little to guide in offering a forecast. Pericarditis may develop insidiously without marked rise of temperature or other symptoms; the temperature may on the other hand remain unchanged by pericardial involvement in the presence of the primary disease.

With *pyemic* and *septic pericarditis* the advent may be heralded by a distinct chill and rise of temperature above the previous level. These chills as in all similar infections are likely to recur, to be followed by fever and excessive sweating, with or without added pericarditis.

Physical signs, i. e., friction sounds, are more dependable than any one other symptom to mark the beginning of the pericardial complication.

If large effusion continues unrelieved during long periods and in cases where after its removal it promptly reforms, the prognosis is bad. These patients fall into a chronic state of invalidism which ends in asthenia with symptoms of compression.

Among the *unfavorable symptoms* are unusually *large effusions,* marked *dyspnea,* advanced *myocardial weakness, small, feeble, erratic and rapid pulse,* the *pulsus parodoxus in cases with thickened pericardium, cyanosis, delirium, coma, albuminuria with scanty urine* and evidences of *septic nephritis, marked tremor, and in children persistent vomiting, hiccough and increasing anemia.*

The *prognosis during early life is under all conditions less favorable* than in the adult. *In children under ten years of age most pericardial effusions are purulent. Mediastinal lesions with pericardial inflammation or extension of mediastinitis to the pericardium* often lead to dense and

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troublesome adhesions and heart weakness. These cases are likely to be subacute or chronic; reference is again made to them under *"adherent pericardium."*

The duration of the disease depends upon the nature of the primary infection. The average case runs its course in from 14 to 21 days, but there are so many factors to influence the complication that it is never safe to commit oneself to a time limit.

In but few cases does pericarditis *per se* lead to death.

Evidences of heart weakness, including dyspnea on exertion, fatigue, syncope, and erratic heart action may continue long after the beginning of convalescence.

Valvular Lesions and Pericarditis.—Gerhardt, C., calls attention to the frequency of *pericarditis with valvular disease of rheumatic origin.* The evidences of endocarditis may remain unrecognized until the pericardial effusion has been absorbed. He further accents the fact already mentioned that in the presence of chronic valvular lesions pericarditis may arise without known cause insidiously, and may lead to permanent myocardial damage. The frequent association of pericarditis and aortic valvular disease was shown in an analysis of 197 rheumatic cases with pericarditis in 17, and in 13 of these, the aortic valve was involved, once alone, in nine cases the aortic lesion was not prominent, in only four cases was the disease limited to the mitral valve alone. The relatively infrequent involvement of the aortic valve with rheumatism would, from Gerhardt's anatomic experiences prove the greater tendency to complicating pericarditis with lesions of the aortic valve, the nearness of the overlying pericardium may be an important factor.

Pericarditis complicating old heart lesions, chronic valvular defects or myocarditis is always serious. In these cases it matters little what the primary cause of the pericarditis may be, the heart revolts, becomes rapid, dilates, there is pulmonary engorgement, general venous stasis, cyanosed kidney and unless treatment proves promptly efficacious, death results.

In many cases the *sequelae of pericarditis* interfere with comfort and the prolongation of life. There may be adhesions, distortion and consecutive interference with the functional power of the heart which may finally lead to irreparable myocardial weakness.

2. Adherent Pericardium

(*Chronic Pericarditis, Mediastinopericarditis*)

Adherent pericardium results from either acute or subacute inflammation. Stokes, Gardner and Walshe understood the results of pericardial adhesions.

Their consideration of the results of adherent pericardium is unequaled

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by anything which has appeared since, with the exception of Broadbent's treatise on the subject.

Barlow and Chevers were agreed that hypertrophy and dilatation of the heart were not necessary sequences of *obliteration of the heart sac* or uncomplicated adherent pericardium.

Walshe proved that after adhesions an atrophic condition of the muscle was more likely to result. In the light of more recent clinical data as reported by Krehl and Romberg, with pathologic observation, the fact is fully corroborated that *hypertrophy or dilatation never follow complete obliteration of the pericardial spaces and that the heart itself may not be unfavorably influenced.*

With mediastinopericardial and pleural adhesions, fixation of the heart to the thorax, and the systolic retraction which is associated with adherent pericardium, immobile thorax often follows. The heart is forced to overexert, it dilates, it hypertrophies and may finally break; marked fibroid and atrophic changes follow. This is most likely to occur with associated valvular defects.

In some cases, particularly where there are mediastinal pleuropericardial adhesions, the x-ray examination will offer valuable assistance.

With *mediastinal, pericardial and pleural adhesions the veins at the base of the heart* may be compressed leading to marked secondary changes in the heart and in distant organs.

Probably the dilatation which exists in a large number of adherent hearts is due more to the diseased condition of the heart muscle than to pericardial interference.

When hypertrophy follows in these cases the *right heart* is usually most enlarged, the hypertrophy becomes a necessity because it must overcome the effect of preceding dilatation. In many cases in which the heart itself is tied down to the chest wall at some point or to the surrounding tissues, the prognosis will depend very largely upon the ability of the heart to help itself by increasing its muscular fibre, hence its systolic strength.

Adhesions early in life interfere materially with the development of the heart.

Adherent pericardium with arteriosclerosis, especially coronary disease, is threatening. The combination may end life without warning.

The heart muscle always remains the paramount issue in the prognosis of adherent pericardium, for in many cases there is either consecutive or preceding myocarditis, as often happens for example with tuberculous pericarditis. Moderate *superficial fatty degeneration of the myocardium,* originally described by Virchow, is not often of serious significance.

Adherent pericardium, mediastinal and pleural agglutination with *added work thrown upon the heart muscle* because of increasing *valvular disease, asthma* and *emphysema, recurring bronchiolitis, kyphosis or pneumonia* (*usually bronchopneumonia*), *advancing arteriosclerosis, chronic*

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interstitial pneumonia (which often follows chronic mediastino-pleuro-pericarditis) becomes a serious condition which continues during long periods to threaten life, usually *with evidences of extreme dilatation* and *dropsies,* and *causes death.*

In connection with *tuberculous pericarditis with adhesions* I mention the influence of the operation of *Cardiolysis of Brauer* on these cases (See Cardiovascular Tuberculosis). The literature of this subject is sufficient with our present experience to prove the enormous influence of the operation of Brauer on adherent pericardium and the *"fixed thorax"*—*"Starrer Thorax"*—of the Germans.

Adherent pericardium with general tuberculosis, valvular disease, nephritis or other grave constitutional defect offers an unfavorable outlook.

Adherent pericardium may persist during many years with but few symptoms and without shortening life.

3. Chronic Pericardioperitonitis

(*Chronic Polyserositis, Pick's Disease, Zuckerguss Krankheit*)

Curschmann and Pick both called attention to productive changes in the serous coverings of the peritoneum, the liver, the spleen, the pleura and the pericardium in which there is enormous fibrous thickening of the various serous coverings with the characteristic appearance which follows the deposit and the drying of a saturated solution of white sugar on a smooth dry surface, to which Curschmann therefore gave the name of *"Zuckerguss Krankheit."*

The various serous membranes seem to be simultaneously affected or the inflammation of one covering may follow close upon the other.

The pericardium may become adherent, the sac obliterated, always with enormous thickening.

Pari passu, with the changes in the pericardium and peritoneum, *ascites* develops. The ascites persists during many years without causing death; to prolong life repeated tapping is necessary. In two cases seen during the past ten years we were obliged to tap on an average of once every four to six weeks. In several of our cases there was hydrothorax and hydropericardium with ascites.

The *spleen* is often much enlarged, its serous covering so thickened as to be unrecognizable.

The *liver* shows organic changes which suggested to Pick the name of *"pericardial pseudocirrhosis of the liver."*

In all of these cases the *obstruction of the portal circuit* is the leading symptom, the evidences of *chronic peritonitis* persist, the pericardium may be deeply involved without causing serious subjective manifestations, but at some stage of the disease the *myocardial weakness* is sure to develop

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and leads to increasing circulatory embarrassment, extensive dropsies, cyanosed kidney and death, unless intercurrent disease interferes earlier.

The *evidences of pericardial thickening and obliteration* may be so few as to make the positive anatomic diagnosis impossible. It may be assumed that with Pick's Disease which has persisted during a long period, the pericardium and multiple serous surfaces are thickened, particularly if the patient is an alcoholic and with recurring ascites shows evidences of myocardial weakness with pleural changes.

One of our cases lived over twenty years and died as the immediate result of an ill advised laparotomy, the surgeon having diagnosed tuberculous peritonitis.

One boy who came to the hospital when about 12 or 13 years of age was observed during eight years and disappeared.

The average length of life is between ten and fifteen years, during which paracentesis abdominalis and in some cases repeated aspiration of the thorax are necessary to prolong life.

Patients who do not die of myocardial degeneration usually yield to intercurrent disease, pneumonia frequently. The process being multiple, radical surgical interference offers no encouragement. I have found death hastened by it.

4. Hydropericardium

The accumulation of fluid in the pericardial sac when non-inflammatory in its origin is usually the result of *stasis, interference with the normal emptying of the veins and lymphatics of the heart, an accompaniment of all possible heart lesions, changes in the walls of the blood vessels due to constitutional diseases, including the anemias and leukemias, hydremic conditions and chronic nephritis.*

The *fluid* is usually of low specific gravity, often contains *sugar* and *chyle.*

With heart lesions and hydropericardium there is usually *dilatation of the ventricles.*

The prognosis of hydropericardium is grave because it depends entirely upon an underlying cause which is usually serious; the accumulation is likely to be a terminal complication.

5. Hemopericardium

The presence of pure blood in the pericardial sac may be due to traumatism, to the rupture of small or large pericardial vessels, to the rupture of an aneurism, either of the heart, aorta or coronary artery or other large vessel, including the pulmonary artery, also malignant growths.

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With hemorrhages of considerable size, collapse is prompt, anemia characteristic, the pulse small and death not long postponed. Compression of the heart by the surrounding blood is an important factor in causing death.

6. Pneumopericardium

This condition is exceedingly rare. I have no record of a case in my own practice. Walter James collected 38 cases of which 26 died.

Traumatism, rupture of esophageal or gastric cancer, surrounding abscess or ulceration, instrumentation followed by accidental perforation of the esophagus, trachea or lung, empyema, pyopneumothorax with tuberculosis and adhesions, have been known to cause pneumopericardium.

The effect on the heart depends upon the cause of the pneumopericardium. External causes leading to prompt surgical interference, improve the patient's chances of living.

Internal perforations promptly lead to suppurative (purulent) pericarditis and usually to death.

When for some reason a small amount of air enters the pericardium without causing purulent or other pericarditis, it may be absorbed without interfering with the functions of the heart and unless the underlying cause is serious the patient is likely to recover.

7. Neoplasms of the Pericardium

The leading new growths of the pericardium are *tubercle, carcinoma, sarcoma* and *gumma.*

Tuberculous pericarditis is separately considered; it is always secondary to disease in other organs (See Cardiovascular Tuberculosis).

When *cancer* invades the pericardium the disease is likely to extend from the immediate neighborhood.

The larger number of *sarcomata* of the pericardium are spindle or round celled and never primary.

Gummata of the pericardium are always associated with myocardial syphilis, either single or multiple, with muscle degeneration.

All new growths of the pericardium cause some symptoms of pericarditis, usually with effusion which is blood stained or purulent.

The prognosis of pericardial new growths is absolutely bad.

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D. Congenital Defects of the Heart

The leading congenital defects which interest the clinician are:

1. *Stenosis of the Pulmonary orifice.*
2. *Defective Ventricular Septum.*
3. *Perforate Foramen Ovale.*
4. *Dextrocardia.*
5. *Stenosis of the aortic orifice.*
6. *Insufficiency and stenosis of the mitral and tricuspid valves.*
7. *Transposition of the aorta and pulmonary artery; perforate and premature closure of the ductus arteriosus.*

It is by no means easy to diagnosticate with anatomic precision the location of congenital defects in all cases where one or more exist, for the subjective and objective manifestations of all are much the same and several are likely to be present in many cases.

1. Stenosis of the Pulmonary Orifice

Stenosis of the Pulmonary Orifice causing obstruction of the pulmonary valve with narrowing of the conus arteriosus of the right ventricle is the most frequent of all congenital heart defects (60 per cent). Of those who live with congenitally defective hearts after the twelfth or thirteenth year, over 80 per cent show pulmonary stenosis. *When only moderate, and stenosis of the pulmonary orifice or the vessel exists, without other defect, compensatory hypertrophy of the right ventricle* makes it possible in the absence of added complication for the subject to live many years in good health. These patients are often conscious of the murmur, but disregard it and are not materially inconvenienced.

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If with pulmonary stenosis there is perforate foramen ovale—a frequent combination—the patient's chances of living are materially reduced. It is unusual for such patients to live beyond the fifteenth year; to live longer is exceptional.

With stenosis and a defect in the intraventricular septum, life is rarely prolonged beyond puberty. Most of these die during the first years of life. The right ventricle hypertrophies enormously to send the blood into the aorta.

With pulmonary stenosis, patent interventricular septum and open foramen ovale the forecast is graver than with stenosis alone. Peacock says "the open state of the foramen ovale and the imperfection in the ventricular septum, so far from adding to the danger, really afford the means of relief to the overcharged right auricle and ventricle without which life could not be prolonged for any considerable period." This "relief," however, is comparative and under the slightest stress or with complications proves insufficient.

Congenital pulmonary stenosis is usually coexistent with auriculoventricular lesions or other evidences of fetal endocarditis.

Fetal endocarditis is not infrequent and is a cause of congenital stenosis and other defects (B. Fischer).

Pulmonary stenosis with patent ductus arteriosus (Botalli) leads to early death. Colbeck says "life is rarely prolonged beyond the thirteenth year."

Complete occlusion of the pulmonary artery leads to early death.

With a high degree of stenosis the blood which reaches the lungs must pass from the aorta through the ductus arteriosus which latter remains open.

When stenosis of the pulmonary orifice is the only congenital defect, there is a fall of pressure in the pulmonary artery, the pressure in the pulmonary veins is elevated, also in the right ventricle with consecutive hypertrophy of both right auricle and ventricle. In many of these cases there is marked cyanosis. In some cases tricuspid insufficiency is superadded.

Pulmonary stenosis and perforate foramen ovale with closed interventricular septum was found by Abbott in 12 per cent of her cases of congenital heart lesions. This makes it possible for much of the blood to find its way along the channel of least resistance through the opening from the right to the left auricle without going through the lung. Naturally the *amount of cyanosis will then depend upon the quantity of blood which finds its way through the lungs via the pulmonary artery.* When these conditions prevail, it takes but the slightest added effort, such as exercise, overeating and emotion, leads to prompt increase of cyanosis and dyspnea.

Peacock found that 74 of 101 of his cases were "blue babies" *morbus*

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coeruleus) at birth, or they showed characteristic cyanosis before the end of the second year.

Cyanosis, dyspnea, convulsions, headaches, clubbed fingers and polycythemia are the leading features of this and most congenital anomalies with associated physical signs.

Nosebleed and purpuric conditions are also frequent.

(For a detailed account of the physical signs of congenital heart defects and further pathologic data, the reader is referred to Hirschfelder's classic work on "Diseases of the Heart and Aorta" (Lippincott, Philadelphia and London) and Maude Abbott's article (Vol. IV. Osler's Modern Medicine).

Almost all who live long enough with congenital stenosis of the pulmonary orifice develop pulmonary tuberculosis.

Abbott reports 80 per cent. B. Fischer (personal communication) says that all who live beyond the fifteenth year show tuberculous changes in the lungs.

Increasing enlargement of the liver, spleen, with cyanosis, albuminuria and ascites in the average case do not continue long before death follows.

Blood counts during all stages of all congenital defects are interesting. The polycythemia of pulmonary stenosis with septum defects may reach as high as 9,000,000, even higher.

Hirschfelder gives Stoelker's statistics showing "53 cases with 32 deaths at birth, 12 during the first year and 11 during the first decade. Only 4 reached the fourth decade."

Abbott's statistics are also quoted by Hirschfelder.

Age at Death.	Pulmonary Stenosis.				Pulmonary Atresia.	
	Ventricular Septum Closed.	Foramen Ovale Closed. Defective V. S.	F. O. Patent Defect V. S.	Ventricular Septum Closed.	Foramen Ovale Closed Defect V. S.	F. O. Patent Defect V. S.
Before 1 year.....	0	4	3*	6	2	10*
1- 7.....	2	16	8	0	3	0
7-14.....	4	5	4	0	0	0
14-20.....	3	8	5	0	0	0
20-28.....	6	3	0	0	0	0
28-45.....	1	0	0	0	0	0
	16	36	20	6	5	10
			*9.7 per cent.			*78 per cent.

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2. Defective Interventricular Septum

We have referred to the defects of the interventricular septum in the preceding paragraphs. The defect was an accompaniment of other anomalies in 78 per cent of Abbott's cases (149). In 58 per cent of these there was stenosis or atresia of the pulmonary orifice or artery. In 24 cases, i. e., 16.1 per cent the ventricular septum defect was uncomplicated. We are rarely called to offer a prognosis in cases of defective ventricular septum for the condition *per se* is not usually diagnosticated. The defects which are coincident, justify the prognosis given in considering stenosis of the pulmonary orifice with this complication. Uncomplicated defects of the septum have been found post mortem in subjects as old as fifty years.

3. Perforate Foramen Ovale

Uncomplicated perforate foramen ovale is the least serious of all congenital defects; it may not cause symptoms. There are many cases in medical literature showing life to have remained uninfluenced; death being due to other causes. The influence which the open foramen exerts on the more frequent pulmonary stenosis is considered in the preceding paragraphs.

Associated mitral lesion may lead to recoil of blood from the left to the right auricle, to venous stasis and cyanosis—a serious and life-threatening complication. *Emboli* may form and reach the pulmonary artery from the left ventricle and pass to remote parts of the body causing fatal infarcts.

4. Dextrocardia

Dextrocardia, without other serious lesions, is usually associated with the transposition of other viscerae and exerts little influence on life. It has been thought by some to predispose to acute infections but there are no positive data which bear on the subject.

5. Stenosis of the Aortic Orifice

Stenosis of the aortic orifice may be due to *fetal endocarditis* or to the congenital displacement of the aortic septum and the unequal division of the aorta and pulmonary artery.

The result of stenosis of the aortic orifice is invariably hypertrophy of the left ventricle. If the aorta is completely closed, the left ventricle remains undeveloped and the circulation is carried forward through the right ventricle assisted by the perforate ductus arteriosus. The prognosis is grave, but few survive birth. Abbott found this defect in 2 per cent of her cases.

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The length of life of subjects with stenosis of the aortic orifice depends largely on the narrowness of the opening and the associated lesions. If the interventricular septum is patent but few live after the ninth or tenth year.

Stenosis of the first portion of the aorta and stenosis of the arch of the aorta at the ductus arteriosus may develop congenitally. Abbott reports this lesion in 198 of her 412 cases—a common anomaly therefore. With a well compensated collateral circulation life may not be shortened, though the heart may suddenly revolt, the *peripheral vessels dilate* and tire, offer no assistance, cerebral hyperemia may prove serious and fatal.

6. Insufficiency and Stenosis of the Mitral and Tricuspid Valves

Insufficiency and Stenosis of the mitral and tricuspid valves of congenital origin depend upon fetal endocarditis. Romberg calls attention to the fact that complete closure of the tricuspid may exist when the blood is conveyed through the perforate foramen ovale and a slit or leak in the ventricle.

7. Transposition of the Aorta and Pulmonary Artery Perforate Ductus Arteriosus and Premature Closure (Botalli)

Occasionally transposition of the aorta and pulmonary artery with or without transposition of the auriculoventricular valves is found. In some cases there is either absence or partial deficiency of the septum between the aorta and pulmonary artery allowing the two vessels to communicate.

The ductus arteriosus normally closes within the first week after birth; failure to close leaves the opening between the aorta and left branch of the pulmonary artery.

Patent ductus arteriosus as already mentioned is, as a rule, combined with pulmonary stenosis or aortic narrowing.

Uncomplicated patent ductus arteriosus may give rise to no symptoms, and may not interfere with life; its presence remains unsuspected and is discovered post mortem. When uncomplicated, the symptoms are not continuous but recurring cyanosis and dyspnea may at times prove troublesome.

Transposition of the aorta and pulmonary artery promptly leads to death; it is incompatible with continuance of extra-uterine existence.

It is often surprising to find the subjects of congenital heart defects

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looking robust; the lesions are irreparable and as Adelman has recently said, they remain "infaust," "the sword of Damocles hangs over these children."

While the lesions do not heal, the physical signs may often change, murmurs disappear or their character is modified.

Most congenital heart defects show insufficiency at birth and therefore many die during the first month of life or shortly after.

If life is prolonged beyond the first year they may live for several years without severe symptoms because of a degree of compensation. The heart muscle becomes an important factor.

With increase of weight, extra work is thrown upon the crippled organ to meet the demands of development, and a break is likely to follow.

Tuberculosis and other pulmonary complications are the most frequent causes of death in those who live beyond the eighth or tenth year. Tuberculosis, the most frequent complication of pulmonary stenosis, does not develop during the first years of life.

Death may take place while children are crying or exercising, during excitement, emotion, from acute, often insignficant infection, during convulsions or with other cerebral complications.

In many cases, repeated *x-ray examinations* will prove of inestimable value for both diagnostic and prognostic purposes; by this method compensatory efforts can be watched.

Each case demands separate consideration; there are no rules which are of value; extreme pictures may improve temporarily, cyanosis and dyspnea threatening at one time may disappear to recur later.

Severe dyspnea and persistent cyanosis with edema are always unfavorable.

Cyanosed kidney, scanty and albuminous urine or nephritis are unfavorable complications.

The character and frequency of the pulse, i. e., *the condition of the heart muscle remains the most prominent prognostic guide with congenital as with all other heart anomalies.*

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E. Diseases of the Myocardium

The myocardium influences prognosis oftener than does any other organ of the body.

In this chapter I consider those conditions which are associated with change of myocardial function usually due to degenerative and toxic, rather than to inflammatory lesions.

It is repeatedly demonstrated in this work that with many constitutional conditions the *myocardial degeneration or cardiac toxemia is the direct cause of death.*

It is unnecessary to repeat in this chapter what is thoroughly considered in connection with the myocardial changes as they complicate the separate infections diseases; to these the reader is referred for details. The same may be said of the results of myocarditis or, more properly speaking myocardial degeneration as found in the *majority of lesions of the heart, including the endocardium*, and *the valves.* These are also separately considered.

I have aimed to impress upon the clinician the overpowering influence of the myocardium in the prognosis of all internal diseases whenever involved.

The *hypertrophy and dilatation* of the heart resulting from, or associated with *valvular defects, arteriosclerosis, kidney lesions, syphilis* and many other individual diseases have also received separate consideration.

Idiopathic Hypertrophy of the Heart.—There are cases of idiopathic hypertrophy of the heart in which the most careful search fails to show valvular lesions, arterial or kidney disease. No cause can be given for many of these hypertrophies. Some of these die with dilatation after a period of cardiac asthenia, including the usual features of broken compensation. In occasional cases there may be few *pericardial adhesions.* In some of these cases death is caused by *bullet shaped thrombi which, as Jores showed,* form by predilection between the trabeculæ of the right ventricle. These cases of idiopathic hypertrophy of the heart ultimately prove to be due to *degenerative and myocarditic lesions.*

There is another type of idiopathic hypertrophy in which both halves of the heart are enlarged, dilatation is not marked, it is usually absent, the heart muscle is of a reddish brown color without characteristic microscopic appearances. There may be stasis in vital organs, there is usually slight arteriosclerosis of *the abdominal aorta and of the renal arteries. Neither the arteriosclerosis nor the renal lesions are sufficient to be considered causative of the hypertrophy.* These cases strengthen the theory of Bollinger that cardiac hypertrophy and arteriosclerosis are "coördinate processes of the same cause."

Idiopathic hypertrophy is often associated with polycythemia, very

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often in alcoholics and without arterial and kidney changes. This condition is frequent in beer drinkers, the heart may ultimately become fatty.

Idiopathic hypertrophy is also found in growing children without known cause. Most of these subjects finally develop dilatation which continues during a varying period and leads to death.

The following lesions of the myocardium will be considered:

1. Acute Purulent Myocarditis.
2. Acute Interstitial Myocarditis (Parenchymatous Myocarditis).
3. Chronic Myocardial Insufficiency.
   - (a) Fibroid degeneration (including the arhythmias).
   - (b) Fatty heart.
   - (c) Fragmentation and Segmentation.
   - (d) Brown Atrophy.
   - (e) Coronary sclerosis with associated myocardial degeneration. (Angina Pectoris.)
   - (f) Senile Heart.
4. Hypertrophy and Dilatation due to,
   - (a) Overstrain.
   - (b) Hypertension.
   - (c) Secondary to lung diseases, asthma, kyphosis, fixed thorax, and non-valvular heart lesions.
   - (d) With masturbation, uterine fibroids and Hyperthyroidea.
5. Stokes-Adams Disease.
6. Syphilis of the Heart.
7. Heart Weakness due to insufficient exercise.
8. Inherent muscular weakness.
9. Insufficiency with the anemias, metabolic faults and toxic states.
10. Neoplasms.
11. Parasites.
12. Rupture of the Heart.
13. Aneurism of the Heart.

1. Acute Purulent Myocarditis

Acute purulent myocarditis is of septic embolic origin; it is usually an accompaniment of malignant endocarditis, localizes itself as a rule in the right conus arteriosus and in the papillary muscles of the left ventricle, *may lead to embolic abscesses, necrosis and even to heart rupture by ulceration.* The prognosis is always unfavorable, death follows a period of positive symptoms including petechiæ and the other usual manifestations of septic endocarditis.

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2. Acute Interstitial Myocarditis

(*Parenchymatous myocarditis*)

Acute interstitial myocarditis and parenchymatous myocarditis may be:

(a) Simple acute interstitial myocarditis,
(b) Acute septic interstitial myocarditis.

(*a*) *Simple Acute Interstitial Myocarditis*

(Romberg)

These conditions have been fully considered in connection with diphtheria, typhoid fever, scarlet fever, smallpox, gonorrhea, rheumatism, measles and other infectious diseases. In some cases the *parenchymatous changes* are in the ascendency. Some are of the mixed type showing both interstitial and parenchymatous changes. *The prognosis depends largely on the virulence of the primary infection.*

(*b*) *Acute Septic Interstitial Myocarditis*

Acute septic interstitial myocarditis is almost always fatal.

It is a serious question whether the differentiation made by Aschoff of (1) *Acute purulent myocarditis* and the (2) *Acute interstitial septic myocarditis* requires consideration for clinical purposes. *Anatomic diagnosis during life is impossible.* The prognosis of both of these septic processes is unfavorable.

3. Chronic Myocardial Insufficiency

(*a*) *Fibroid Degeneration*

("*Weak Heart*," *Debilitas cordis, Myodegeneration of the Heart, Myocardial degeneration*)

Myocardial degeneration is the most frequent of all lesions of the heart causing death. It is a disease of advanced life; when found early in life it usually leads to prompt death if not due to syphilis. Women are not as often affected as men, and when they are the disease shows itself later than in men. The heart lesions which are increasing with surprising rapidity are of a degenerative fibroid character, they progress insidiously without marked physical or subjective symptoms during a long period; the patients present for treatment as a rule, after the initial stage, when complex conditions exist.

It may be assumed that the *degenerative process* is brought about by interference with the proper nourishment of the heart muscle through the *coronary arteries.* The result is *sclerotic or fibroid* change in the mus-

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culature of the heart. The heart in these cases passes through a period during which it is overtaxed because of faulty pabulum to its muscle elements and there is usually a long existing and unrecognized hypertension with added toxic conditions.

The influence of *faulty metabolism, long continued worry and strain, syphilitic infection and obstructive changes in the peripheral capillaries* as found with arteriosclerosis of the kidney and mesenteric vessels is of paramount importance for prognosis and etiology.

An overworked heart with peripheral obstruction and associated high blood pressure is likely to yield when extra demand is made upon it. This is particularly true when there is advanced coronary disease. *Cases detected in the initial stage* without marked distant (arteriosclerotic) changes and not progressive, which are tractable and able to follow the directions of the physician, are often favorably influenced by treatment. The prognosis will depend entirely upon the associated conditions, the capacity of the myocardium, which can be tested by safe methods, the age of the patient, and the underlying cause.

Conditions are often complex even in the early stage of myocardial weakness and in many cases make prognosis exceedingly difficult, often impossible.

If during the initial stage there are attacks of stenocardia (angina pectoris) and these are severe, the chances of materially prolonging such a life are small (See Angina Pectoris).

Early evidences of stasis, particularly enlarged liver and spleen with cardiac asthma are among the unfavorable features, as are also dyspnea and symptoms referable to the peripheral vessels.

It is unfortunate for many of these cases that the patient is often unconscious of myocardial disease until the heart reserve has been exhausted. The symptomatology associated with similar lesions is so variable in different cases, as to mislead the clinician and the patient. Mackenzie says that "at first sight the 'symptoms' are hopelessly confused." "I have submitted to Professor Keith a large number of hearts affected by the changes associated with arteriosclerosis from patients ranging from forty-two to seventy-seven years of age, and in all the post mortem appearances had such a close resemblance that it might have been assumed, that during life the symptoms would have been identical." This however is not the case. Some patients suffer from serious anginous attacks and in the intervals present no evidences of myocardial disease, while others with exactly similar lesions present the continuous symptoms of muscular weakness; still others present no evidences of any lesion in either subjective or objective symptoms, but suddenly, there is either an acute dilatation, a pulmonary edema, the development of arhythmia, extra systoles, suddenly arising evidences of extreme muscular insufficiency, the pulsus alternans and prompt death. Others develop dropsies,

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while with exactly the same lesions there are often no dropsies. The functional disturbances therefore are differently influenced in different cases by the same lesions. It is impossible for the physician as Allbutt has said to draw a parallel "in the living patient between the formidable works of decay described by the pathologists; how and when these degenerations are manifested; how, in the long course of cardiac decay the imminence of death is to be foreseen and provided against; or how, indeed, we are to know that any such process is at work at all; or lastly, how in a case of known heart disease the degrees of its advancement and of the cardiac reserves are to be noted and tested." "Thus we have the physician and the pathologist trotting each on his own side of the hedge, each intent upon his own scouting and his own bearings, and neither able as yet to reconcile his own observations with those of his comrade."

The blood pressure study of fibroid degeneration offers varying results. Early high blood pressure (hypertension) *with symptoms of myocardial degeneration sufficient to make the diagnosis possible is as unfavorable as hypotension with the same subjective complaints.*

Sudden decided fall of blood pressure with small and rapid pulse and distant heart sounds is always evidence of insufficient heart power. High blood pressure, without evidences of coronary involvement in subjective symptoms, without aortic insufficiency, without arhythmia, with or without an aortic systolic murmur, but with the pulse pressure approaching the normal (40 to 60 mm. Hg.) *may be considered favorable for the continuation of life,* and the patient is often able to continue his occupation if it is not too taxing, mentally or physically. These patients are materially influenced by *autosuggestion;* the personal element plays an important rôle, and the prognosis is often improved by the tactful consideration of existing conditions with abundant and justified reassurance and the judicious planning for the future.

Too much importance has been given to systolic blood pressure by the lay world, often by the physician, without a just estimate of the many collateral conditions to be considered in all cases of myocardial degeneration.

High systolic blood pressure with myocardial fibrosis in patients beyond 55 years is often without unfavorable effect. There is a class of cases in which the myocardial degeneration progresses rapidly; it includes men who work under unusual strain who often develop hypertension which is promptly followed by hypertrophy of the left ventricle, and for some reason the associated kidney cirrhosis progresses with equal rapidity. The prognosis of these rapidly developing cases is bad. The duration of some, from the beginning of the subjective symptoms which brought the patient to the physician to the end, has been less than four months. These are exceptional conditions. The *revolt of the myocardium in the terminal stage* is associated with dyspnea, erratic heart action and nocturnal pulmonary edema in some, cardiac asthma in others.

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Early evidences of edema are not encouraging neither are the symptoms of stasis within the portal circuit (*Liver engorgement and gastritis*).

Pallor with vertigo arising suddenly, with or without arhythmia, particularly on slight exertion, are warnings of weakness, which when unheeded lead to serious results, at times ***sudden death.***

Physical signs which show marked dilatation and embryonic heart sounds in any stage of fibroid or any other form of myocarditis are always suggestive, worse with dilatation of the left than the right ventricle. With *angina pectoris* and *myocarditis* the ventricles are not dilated as a rule, though the outlook may be exceedingly grave.

With *emphysema, chronic bronchitis* and *marked kyphosis* the evidences of right ventricular dilatation are often borne during long periods and with improved conditions (often possible) the dilatation disappears.

Accented second pulmonic sound is always evidence of insufficiency of the mitral valve and with fibroid degeneration the insufficiency is likely to be relative.

The *advanced and unfavorable symptoms* often follow an acute exacerbation; an *anginous seizure or a suddenly arising cardiac asthma,* or *nocturnal pulmonary edema may be followed by continuous symptoms of decompensation. Severe dyspnea* may persist after such acute attacks and may never disappear. In a number of cases *evidences of stasis in the liver* and *dropsies of the serous cavities* (*hydrothorax, hydropericardium,* occasionally *ascites* and *edema of the extremities*) develop; marked *arhythmia* becomes continuous, there is *albuminuria with reduced urine, excessive nervousness, finally orthopnea and death ends the scene.*

Physical examination of the heart in the terminal stages shows marked dilatation of the left ventricle; systolic murmurs over the mitral and aortic areas are frequent, the second pulmonic sound is accented and with hypertension and interstitial nephritis the second aortic sound is also snappy and loud.

In another class of cases the heart is so exhausted that the sounds are indistinct, distant and embryonic in character. With increasing weakness, the heart becomes rapid and as already suggested arhythmia is a further evidence of myocardial insufficiency.

There are cases of serious fibrosis of the myocardium in which the pulse gives absolutely no indications of the existing condition—this is of great importance. Even with normal frequency, rhythm and blood pressure, advanced degeneration may be present and increase rapidly.

A normal pulse which is markedly influenced, i. e., accelerated by slight exertion, is always suggestive of myocardial degeneration. *Persistent rapidity, as well as marked* ***bradycardia*** *and instability as shown by decided variation in the frequency and character of the pulse are serious.* Experience teaches that *a heart which has been overtaxed or in which a lesion has been recognized which suddenly becomes erratic or shows that*

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its reserve is being reduced by the development of any form of arhythmia, is an organ which demands a guarded prognosis. Many such hearts may again "find themselves," but they are not dependable, such organs are easily fatigued, they revolt on slight cause, are likely to desert when but little overtaxed, they dilate unexpectedly. On the other hand favorable cases are met which after serious evidences of weakness regain sufficient force to live in comfort with proper care during long periods. "In no organ is this lack of concord between the signals of life and death so disconcerting as in the heart." (Allbutt.)

The Arhythmias

The irregularities of the heart which interest the clinician in connection with myocardial degeneration are:

(i) Sinus irregularities.
(ii) Irregularities due to depressed conductivity.
(iii) Irregularities due to extrasystoles (premature contractions).
(iv) Pulsus alternans.
(v) Auricular fibrillation.

By the use of *graphic methods* we are now able to gain information for diagnosis and prognosis which have metamorphosed cardiac pathology. By the simultaneous study of the jugular and the arterial pulses we now obtain a clear conception of the clinical significance of, and the factors which cause the arhythmias.

In this work we concern ourselves with the prognostic significance of the separate arhythmias, basing our conclusions on the work of Mackenzie, Lewis, and Price.

i. *The prognostic significance of Sinus irregularities*

The usual form of sinus irregularity is of little prognostic significance. Lewis excludes "the prolonged and sudden cessation of the heart beat and the true phasic variation of pulse rate." *Sinus irregularity is not frequent with myocarditis* but is usually found in young subjects and in those who have been taking digitalis.

ii. *Irregularities Due to Depressed Conductivity*

We do not include all of the fully developed Stokes-Adams phenomena in this consideration. (See Adams-Stokes Complex.)

The prompt impulse along the auriculoventricular bundle is disturbed or delayed with depressed conductivity. Price suggests three grades of impairment: (1) The stimulus from auricle to ventricle is merely delayed—that is, there is merely a prolongation of the interval which sepa-

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rates the commencements of contraction of the auricle and contraction of the ventricle. (2) The stimulus does not at times cross over; in other words, the ventricle does not at times respond to the stimulus from the auricle (this is called *"partial heart block"*) and (3) no impulses at all reach the ventricle from the auricle, so that the auricles and ventricles beat quite independently of each other, the ventricles at an approximate rate of 30 per minute ("complete heart block").

Our clinical experience teaches that heart block of any form with myocarditis is a serious condition, it certainly indicates a diseased and weakened myocardium.

In all forms of irregularity due to depressed conductivity there is great danger from *sudden cerebral anemia* and *revolt of the heart muscle which may lead to sudden death.* We are not considering the temporary dissociation of febrile disease in which the prognosis is fairly good, but the graver condition which is due to an organic and permanent change in the myocardium.

iii. *Irregularities Due to Extrasystoles*
(*Premature Contractions*)

Extrasystoles represent the commonest of all intermissions—an extrasystole is a premature contraction either of the auricle or ventricle or of both together, while the sinus rhythm is maintained.

The *normal rhythm of the heart* is interrupted by either frequent, or occasionally by a premature beat; the following pause is abnormally long which is termed the "compensatory pause." The beat which follows is more powerful because of the long period of rest after the extrasystole.

The *pulsus bigeminus* is due to a regularly recurring extrasystole after each normal heart beat.

Feeble extrasystoles may not be felt at the wrist, the pause simply is recognized as *"dropped beat" or intermittent pulse.*

Extrasystoles are most frequent during middle life and directly after, in men oftener than in women, and oftener with fibroid myocarditis (cardiosclerosis) than with valvular disease. The Mackenzie school does not consider extrasystoles as bearing seriously upon prognosis. The consensus of the modern school is summed up in the following quotation, "Unfortunately the public has come to attach a serious significance to them, (extrasystoles). This is absolutely without foundation. When extrasystoles are considered by themselves, that is, without reference to the condition with which they may be associated—there is no evidence for supposing that extrasystoles can be taken as an indication of an impaired heart or add to the gravity of an already diseased heart." (Price.) To this Mackenzie and Lewis subscribe. *We are, however, dealing with myocardial fibrosis, and while many cases live for years with extrasystoles*

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the arhythmia must be considered indicative of a diseased myocardium and should never be disregarded though its importance is less than are most other arhythmias. I know that extrasystoles accompany grave heart lesions and safe reasoning leads the clinician to the conclusion that the associated lesions must give their own prognostic indications. *We do not deny the possibility of a healthy heart falling into the bad habit of producing premature contractions.* The work of the degenerated heart muscle will certainly be increased finally by the presence and persistence of extrasystoles, and in direct proportion to their frequency—Lewis, it seems to us offers the safest conclusion. "Premature contractions constitute and bear witness to defects" . . . "*while premature contractions have unquestionably a relatively insignificant import, as compared to* many forms of cardiac irregularity, entire neglect of their presence is not advisable."

iv. *Pulsus alternans*

With the alternating pulse, the heart beats regularly, but each alternate beat is larger than the beat immediately preceding, hence with the contraction of the left ventricle the quantity of blood thrown into the aorta is larger and smaller at alternate contractions. The size of the pulse is necessarily influenced and the tracings are correspondingly clear.

Alternate pulse is sometimes found when the heart contracts with unusual frequency as with paroxysmal tachycardia, under such conditions it is less serious than in those cases with which it is most frequently associated, i. e., when the heart rate is not accelerated; the pulse may be of normal frequency or even reduced in frequency with *fibroid myocarditis, angina pectoris, hypertension with chronic interstitial nephritis and in all forms of decomposition associated with dilatation of the heart and fatigue.*

The pulsus alternans is evidence of an overtaxed heart; it means that the heart is struggling to carry its burden, that its reserve is exhausted, and it always adds to the gravity of the case and is always serious. Lewis says "It ranks with subsultus tendinum, with optic neuritis, with the risus sardonicus and other ill-omened messengers. It is the faint cry of an anguished and fast failing muscle, which, when it comes, all should strain to hear, for it is not long repeated. A few months, a few years at most and the end comes." The alternating pulse, being a symptom of advanced myocardial degeneration, is associated with other grave symptoms in most cases, these include *angina pectoris, hypertension, nocturnal dyspnea, often with pulmonary edema or cardiac asthma, Cheyne-Stokes breathing,* or *it may be the only evidence of a crippled myocardium* which suddenly balks when death is entirely unexpected.

"These results support the teaching of Dr. Mackenzie. In his expe-

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rience, the inception of the pulsus alternans in aged people has invariably been followed by fatal heart failure within two or three years." (Windle.)

Windle in his article on "The Incidence and Prognostic Value of the Pulsus Alternans in Myocardial and Arterial Disease" offers the following in

Table 1

Pulse irregularities observed in 202 cases of arteriosclerosis:

Nature of Irregularity.	Number of Cases Observed.	Percentage.
Extrasystoles	109	54.5
Complete irregularity	61	30.5
Pulsus alternans	23	11.5
Impaired a.-v. conduction	3	1.5
Partial heart-block	1	0.5
Complete heart-block	4	2.0
Sinus irregularity	1	0.5

v. *Auricular Fibrillation*
(*Auricular Flutter*)

The "flick" or "flutter" of the auricle with fibrillation is rapid, erratic and is produced by "stimulus production at multiple auricular foci." *A large number of irregularities are due to auricular fibrillation.* The influence of auricular fibrillation on the ventricle according to Lewis is twofold. "The normal regular and coördinate contractions in the auricle are in abeyance and consequently the ventricle is robbed of the regular impulses which form its accustomed supply. These are replaced by numerous and haphazard impulses, escape to the ventricle from the turmoil which prevails in the upper chamber; the change is consequently profound."

The condition is most frequent during advanced life when degenerative processes are numerous.

It is not present during the first decade of life.

It is more frequent in men than in women.

It is a frequent accompaniment of mitral stenosis. Lewis says "*Mitral stenosis and auricular fibrillation are bosom companions.*"

Ventricular fibrillation is promptly fatal, and is the cause of *sudden death* in a number of cases.

Auricular fibrillation is synonymous with muscular degeneration of the auricle and characteristic of advanced changes.

It is the precursor of cardiac surrender in many cases—in other

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cases the heart learns to accommodate itself to the flutter and cases are recorded which lived ten years and longer after the initial seizure.

In some favorable cases the fibrillation is paroxysmal.

The frequency of the beat influences prognosis; the more frequent the flutter the greater the danger of exhaustion.

The results of digitalis treatment on auricular fibrillation influences the forecast. The drug in favorable cases acts as a specific and promptly controls the symptom, if it fails, the prognosis is absolutely bad.

The conclusions of Gossage and Braxton Hicks are appended:

"1. That the exact cause of auricular fibrillation is unknown.

"2. That it usually comes on in a heart where there has been for a considerable period disease of the valves or myocardial change from inflammation or degeneration.

"3. That it sometimes arises suddenly where there has been no previous sign or symptom of heart disease.

"4. That possibly in some of these cases it occurs in hearts which were previously perfectly healthy.

"5. That if this is true its essential cause must lie outside the heart and not in any anatomical or pathological change in the heart itself.

"6. That sudden death in auricular fibrillation is probably due to the onset of fibrillation of the ventricles, and that some cases of sudden death both in diseased and healthy persons may be due to the simultaneous onset of fibrillation of both auricles and ventricles."

The prognostic significance of the Atropin reaction in diseases of the heart has received considerable attention from various sources. The *hypodermic* injection of 1/50 to 1/25 grain of atropin produces a decided increase in the heart rate by paralyzing the pneumogastric. It acts directly on the vagus and not on the myocardium. Cushny first suggested "releasing of the vagus by means of hypodermic doses of atropin, so-called atropin reaction in the study of digitalis action" (Talley).

The polygraph or sphygmograph is used to register the pulse rate and to show the contrast. The rate is to be averaged by ten minutes' observation before taking the hypodermic, the reaction is again averaged by ten minutes' observation, when after the injection, the pulse is at its maximum. The normal reaction is from 30 to 40. Talley should be consulted for a full understanding of the method, his conclusions follow:

"1. The atropin reaction in the normal heart is probably from 30 to 40.

"2. A reaction of 20 or less, in a heart not recently subjected to exhausting disease, points to a degenerative process in the cardiac tissue which makes the outlook for improvement under treatment unpromising.

"3. Cases of auricular fibrillation with normal response or above, are promising subjects for treatment.

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"4. Two atropin reactions in case of auricular fibrillation, one before and one on full digitalis, enable us to determine whether the vagal or the cardiac tissue factor is the greater. The patients with a large cardiac tissue factor are the ones who usually are sufficiently improved by treatment to return to their occupations."

Fibroid myocarditis once established is never cured. It can be controlled in many cases by rational living. Its extent naturally influences the prognosis as well as the course of many associated conditions.

Sudden death occasionally occurs without previous warning of the existence of any lesion. This is not frequent. *But few die in whom a thorough consideration of symptoms and physical examination would have failed to lead to a correct diagnosis.*

Diabetes, gout, and *other diseases,* as well as a *faulty diet for metabolic faults, the use of thyroid extract for obesity, continued mental strain, acute disease, particularly influenza,* often prove depressing factors which promptly invite progression of existing degeneration.

The *fate of the myocarditic patient often depends on his own acts. It is surprising to note how many of these patients with weak hearts (degenerated) continue to live in favorable surroundings and conditions with a minimum of symptoms during many years, when they give the heart the rest which it needs.*

Errors of diet, excesses of any kind, may promptly shorten life, which with rational treatment, temperance and sobriety might have continued during a considerable period.

The effect of tobacco, tea, coffee, alcohol and *sexual indulgence* demands the closest scrutiny in the individual case, and if the patient wishes to prolong his life, he must be willing to make sacrifices and forego many pleasures.

In favorable cases the effect of rest and treatment is comparatively prompt and is followed by the disappearance of threatening symptoms.

(*b*) *Fatty Heart*

Fatty disease of the heart may be due either to the *accumulation of fat in the subpericardial tissue, which may also deposit between the muscular fibers of the heart,* a condition found with obesity, at times with carcinoma and tuberculosis, or to the *"fatty degeneration of the heart"* in which the muscular tissue has undergone a fatty degeneration, which may be diffuse or more or less localized. The heart cavities are dilated, hypertrophy is impossible in advanced cases because there is insufficient muscle element left; the heart is therefore usually flabby and dilated.

With obese patients the small and feeble organ is insufficient to meet the demands made upon it by the enormous body when the changes are advanced. The association of obesity with coronary sclerosis, and a

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high diaphragm to which Romberg calls attention is an unfavorable combination.

In many obese subjects the two forms of fatty disease are combined.

When with fatty accumulation in obese subjects there is also fibroid myocarditis the prognosis is bad.

In obese subjects with diabetes and gout, a combination which is not infrequent, *or with diabetes alone, the evidences of heart fatigue and insufficiency* may *arise suddenly, and promptly end fatally.*

Whenever an obese patient develops arhythmia suddenly, it is proof of cardiac insufficiency and is serious.

Fatty degeneration of the heart is also found with all wasting diseases, pernicious anemia, with phosphorous poisoning, pericarditis, endocarditis and with the myocarditis of many acute infections.

The myocardial degenerations are not infrequently of the mixed type, i. e., fibroid and fatty degeneration or parenchymatous may be present together.

So long as the heart muscle itself in the obese subject is intact and the deposit of fat in the surrounding tissues is not serious, the danger lies in the invasion of the myocardium—the extent of fatty and fibroid degeneration.

Leyden holds that in such cases dropsies have been overcome. This in our experience is exceedingly rare.

The influence of diet and carefully supervised exercise and the Bergonie treatment is favorable in occasional cases.

With dilated hearts in obese subjects and evidences of stasis, the prognosis is grave.

Arteriosclerosis and obesity with heart symptoms develop conditions which advance insidiously and lead to death.

The increase of dullness to the right of the sternum is less serious than similar increase to the left of the nipple line which is proof of dilatation of the left ventricle. The former is often due to fatty deposit rather than degeneration.

The prognosis of fatty degeneration of the heart is primarily influenced by its cause. With the acute infections under proper precautions it may disappear or cause no further symptoms after fully established convalescence; the same is true of *anemic conditions* which are amenable to treatment.

Feeble and distant heart sounds with dilatation, relative mitral insufficiency, dyspnea, arhythmia, faintness, syncope, cyanosis, and stasis in the abdominal viscera, are among the unfavorable features of fatty heart.

Fatty degeneration due to coronary disease is usually of the mixed fatty, fibroid type and is fatal. Rupture of fatty heart is a frequent cause of death. One such case we met during a gall-stone colic. Sudden *death during gall-stone* or *other colics* (*renal*) is at times due to fatty

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and insufficient heart. In 77 per cent of fatty hearts Hamilton reported spontaneous rupture.

(c) *Fragmentation and Segmentation*

Fragmentation and *segmentation* cannot be diagnosticated ante mortem, they interest the pathologist. The true significance and cause of fragmentation is undecided. Post mortem, the heart muscle with *fragmentation* shows transverse breaks or fractures across its fibers; with *segmentation*, the muscle fibers themselves are separated along the line of contact.

Fragmentation has been found in hearts without degenerative changes and may be due to ante mortem or post mortem changes.

(d) *Brown Atrophy*

Brown atrophy is frequently found with chronic valvular disease in the senile heart and with cachectic states.

The heart is small and usually insufficient. When brown atrophy exists during a comparatively long period fibroid changes are also found in the myocardium.

With the small heart of brown atrophy there is feeble systolic force and hyotension.

The prognosis depends on the cause; brown atrophy can only be suspected during life, never positively diagnosticated.

Starvation Atrophy.—The enormous tolerance of the heart makes full recovery possible after *atrophy due to starvation and long continued wasting disease.*

(e) *Coronary Sclerosis*

(*Angina pectoris*)

Seneca wrote of angina pectoris, "To have any other malady is to be sick; to have this is to be dying."

John Hunter, himself a victim of Heberden's disease and his contemporary, said "my life is in the hands of any rascal who chooses to annoy or tease me."

We have no clearer or more classic picture to offer of angina pectoris than is included in the original description of the disease by Heberden in his Commentaries on the History and Cures of Disease. In the present state of our knowledge reasoning from the prompt appearance of the symptoms of angina when the heart muscle is taxed in those suffering from the disease, whatever the lesion found on post mortem, we are justified in including the complex with the diseases of the myocardium

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and subscribe to the dictum of Mackenzie "that angina pectoris is an evidence of exhaustion of the function of contractility" and that the pain "is a viscerosensory reflex."

Coronary disease is unquestionably the leading lesion of angina pectoris. It is associated in a proportion of cases with *aortic disease—aortic aneurism, simple dilatation of the aorta, aortic valvular disease and in but few cases do we fail to find myocardial degeneration, a result of faulty nourishment through the coronary vessels.*

Hypertension is often associated with some one of the above mentioned lesions, but is by no means a constant attendant of the disease either during the paroxysm or in the interval.

Fiessinger contends that the danger to life of angina pectoris has been somewhat exaggerated and divides cases of the disease into six groups, according to the cause, viz.:

coronary involvement,
aortitis,
myocarditis,
interstitial nephritis,
obesity and
aerophagia—this order of enumeration is that of decreasing gravity.

The *exhausted left ventricle is an important attendant of angina pectoris in all cases.* In most cases the ventricle is struggling against an increased pressure, this relieved, the sensory symptoms are long postponed or may never recur. It has been the experience of all clinicians to find the *fading of anginous attacks with the appearance of ventricular dilatation and mitral insufficiency.* Musser, Broadbent, Mackenzie, Abrams, and Elsner report similar experiences. The heart during the attacks is perceptibly reduced in size; with broken compensation and dilatation the prognosis so far as angina pectoris is concerned is better in direct proportion to the amount of dilatation.

After severe illness, the symptoms of angina pectoris often disappear. Ortner mentions such cases. We include in our series the case of a woman who almost twenty years ago had typical angina with chronic nephritis and advanced aortic lesion. She developed uremia, passive cerebral hyperemia, was unconscious during a long period with a threatening pulse, she finally rallied from the acute symptoms and never again had the slightest suggestion of coronary spasm.

I count among my cases a number of men and women in whom there was complete recovery from anginous symptoms during many years after the development of added heart and kidney lesions. One of these was a clergyman who had severe angina during several months when he was stricken with vague febrile symptoms associated with marked cerebral manifestations; he made a full recovery from these and for nineteen

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years continued at the head of a large congregation when he developed anew the symptoms of angina with nephritis.

I do not consider "*pseudo angina*" a disease *per se.*

There are occasional cases of pain and other associated symptoms in which it may be assumed that there are no lesions in the coronaries or heart muscle but which are due to vaso-constriction or spasm of the arteries, in which the symptoms of stenocardia are of secondary origin. Nothnagel's article on "Angina pectoris vasomotoria" describes these fully. These patients are easily influenced by cold, after and during exposure they have the characteristic pang, and this is likely to persist until they are thoroughly warmed. My experience is in accord with that of Mackenzie that the blood pressure is not high in these cases either during the attack or in the interval. The prognosis of vasomotor angina is more favorable than is that of other forms of the disease.

The enormous increase of stenocardia or coronary disease is striking. This is especially true among professional men. In 6,155 cases of internal disease I found 110 fully developed (1.78 per cent) coronary scleroses. This is in striking contrast to the rarity of the disease during the days of Benjamin Rush; out of his enormous experience he reported in a lecture to his students that he had seen but one case of angina pectoris, and he mentioned the name of a colleague practicing in Philadelphia who had also seen but one case.

Coronary sclerosis may truly be considered "the doctor's disease" for it is more prevalent among physicians than among any other class of men. Over 80 per cent of deaths among the teaching medical faculties of the large universities of the world during the past ten years have been due to this disease. Romberg has said that arteriosclerosis is most advanced in the vessels which are most taxed; physicians tax their hearts and brains most, hence their coronaries and cerebral vessels must bear the burden.

There is no disease of the arterial tree in which family history is a more striking pathogenic and prognostic factor than in angina pectoris. It is not at all uncommon to find several members of a family in which the father or mother had fully developed angina pectoris. With a strong ***family tendency*** *to the disease*, the symptoms, are likely to develop in the fourth decade, occasionally in the third, and the course of the disease is more rapid than when developed later in life.

My experience justifies the statement that *almost all cases of angina pectoris developed before the fortieth year are either associated with a direct hereditary tendency or are of syphilitic origin.* In the subjects burdened with heredity there is usually an *unrecognized period of hypertension* and the development of the complex is hastened sooner than it is in other subjects who are exposed to the same hurry, worry and overwork.

When we consider the prognosis of angina pectoris from the purely

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clinical manifestations which are produced, two pictures stand out in bold relief.

First. The large attack, suddenly arising, usually after excitement, worry or a hearty and full meal, in which the anguish is great, the pain severe, breathing uninfluenced as a rule, a sense of impending death, the sensation of a heavy load resting on the thorax, at times the "heart is pressed in a vise," *blood pressure presents no distinctive features,* it may be high, is usually however nearly normal or may be slightly depressed; the pulse is equally non-committal, it may be slow or normal, if the attack is long there may be extrasystoles; with advanced myocardial degeneration, there may be great rapidity, the pulse small and sometimes alternating. The pulse in many cases seems entirely unchanged from the normal, to the moment of death. The heart may suddenly stop during diastole often at a time when its systolic force seems reassuring.

Second. The small attack. The majority of cases which now present, suffer from the "small attacks"; these are suggestive of the larger attack but are less severe and in many cases, after the disease has continued during a varying period, are likely to recur on slight cause; they are evanescent and the varying sensations described by different patients promptly cease with rest. In the advanced cases the small attacks are promptly provoked by the slightest extra tax on the heart, but they are rarely associated with the severe pain of the larger attacks, neither does the pain often radiate from the sternal regions into the neck or beyond the left shoulder; the patient is not materially weakened by recurrence. Each one of the large attacks has been said to "add a peg to the coffin"; the smaller attacks are often borne during many years without serious results in patients who profit by rational living. The first larger attack may kill the patient; as a rule there are several larger attacks before the fatal termination. The large attack may never recur, the patient may fall into a condition of chronicity covering many years during which he has many small attacks, or several months or years may intervene after which severe attacks follow. It is impossible, in the absence of physical signs, to give a prognosis of value.

No disease presents more prognostic problems than does angina pectoris. "The cardinal fact in real angina is its uncertainty" (Walshe).

The small attacks rarely kill, they make the lives of the victims wretched and uncertain; they do not often interfere (nor should they) with light occupation, and with care the patients may continue to live during many years.

I have found that *the effect of vasodilators offer valuable prognostic data.* Angina pectoris (either large or small) which is promptly relieved by small doses of glonoin, given dry on the tongue, offers a favorable forecast so far as the prolongation of life is concerned. Thus many men who have angina pectoris, by the aid of infinitesimal doses of glonoin are

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able to take exercise and prevent serious symptoms during long periods. This effect is by no means the result of suggestion. The author has given the method too many trials to be mistaken.

Cessation of activity during the first moments of a large or small attack has a favorable effect in most cases.

Large or small attacks recurring during rest or during the night, arousing the patient from sleep are always serious, they indicate advanced disease.

Women bear angina longer and better than do men. They are better able to rest and their worries are fewer and their activities more limited.

Large or small attacks in young subjects unless specific, are more likely to end life sooner than are similar seizures in older subjects. *Arhythmias persisting or arising during attacks are an expression of myocardial weakness.*

Extrasystoles are easily borne during years by many who suffer from the milder form of the disease.

Persistent and intensive antisyphilitic treatment in the presence of a positive Wassermann reaction offers a good chance of complete cure. The number of cases associated with aortitis prove the frequency of syphilis as a cause.

Closure of both coronaries leads to prompt death.

One coronary may be sclerosed during a long time without causing death. The trunks may be atheromatous tracing them into their intramuscular network to find the finer branches free from disease and thus there is sufficient blood to maintain the heart wall and prevent serious revolt.

With aneurism and aortic disease and angina, the prognosis is absolutely bad.

With aortic insufficiency and coronary disease (a frequent combination), there is constant danger and death is not long postponed.

Evidences of aortic (valvular) degenerative change (arteriosclerotic) with coronary disease and small attacks with slight hypertrophy of the left ventricle and a reasonably dependable blood pressure are found in many cases which live for years, are always in danger; they hold their lives in their own hands. Indiscretion is not long tolerated in these cases. An aortic systolic murmur should not always be seriously interpreted, for it is present in many cases which live many years.

A single debauch, a single error of diet, with the overloading of the stomach, may lead to prompt death. These are the cases which are reported by laymen and often by physicians as "acute indigestion." "Acute indigestion" does not kill a man with a normal heart.

Thrombosis or embolism of the coronaries is a frequent cause of death. It cannot be influenced by any known treatment. *Acute dilatation added to coronary sclerosis* either during an attack or in the interval, if extreme,

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is serious; moderate dilatation which may be provoked by forcibly striking the cervical vertebrae with a percussion hammer often relieves the attack and saves the patient. Osler has called attention to angina pectoris as an early symptom of *aortic aneurism.*

Anginoid attacks occur in children with valvular disease and with adherent pericardium. I have seen a number recover, particularly with valvular defects, our experience with adherent pericardium in children has been limited.

In the adult, I saw one case in which *cardiolysis* cured the patient, a physician who is now engaged in active practice.

Angina pectoris of toxic origin offers a favorable prognosis if the coronary sclerosis and myocardial degeneration are not too far advanced.

Tobacco angina is amenable to rational treatment, as are also those indefinite cases attributed to tea, coffee, etc. When symptoms persist in spite of discontinuance of the supposed cause, it may be concluded that grave organic disease exists.

Abdominal angina (*dyspragia intermittens intestinalis et abdominalis* of Ortner) is due to sclerosis of the *superior mesenteric artery*, as a rule; it may alternate with angina pectoris, or the coronaries may not be involved. The prognosis depends on the extent of the general process. With abdominal angina life may be materially prolonged in most cases.

Interstitial nephritis with angina, is usually associated with marked hypertension and advanced arteriosclerosis. In these cases death is not often due to the coronary disease directly; most of our patients have died of *uremia* or *other complications. Sometimes there has been a period of decompensation without recurring angina, but with dropsies.*

In all cases of angina pectoris *excessive coitus*, at times even moderate indulgence, influences the case unfavorably.

Pulmonary edema has complicated a number of our cases immediately following coitus.

Agreeable occupation is necessary in those cases which are about; *idleness and a self-centered state increase all symptoms.*

In no other disease of the cardiovascular system is the patient so promptly influenced by his psychic condition. The exalted and overwrought brain is associated with the tear which often kills these patients.

The painful seizures accompanying Graves' disease yield to treatment. It is questionable whether they belong among the true anginas.

There are occasional neuroses which justify the term "anginoid"; these are all symptomatic and offer a good prognosis. In all cases the condition which caused the symptoms must give the data upon which the forecast should rest. This requires of the physician the most painstaking investigation of all details, a task which is not without its reward. The severest "large attack" in which the life of the patient seems lost may yield and the patient may live to enjoy life, while the "smaller

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attack," almost unnoticed, if neglected may lead to death. This is not the rule. I repeat—the prognosis is unfavorable in proportion to the ease with which the attack is produced by seemingly *insignificant causes,* in cases with *marked arterial degeneration, with hereditary tendencies, with carelessness of the patient,* under *unfavorable surroundings* and *social conditions, failure to rest, with associated progressive metabolic faults, gout, diabetes, lead-poisoning, added acute infections* and with *pneumonia.*

Self cure of angina pectoris is possible.

The revelations of the *Röntgen rays* are needed in all cases to assist in clearing the horizon and often lead to valuable data for prognosis. The task of the physician in conveying to the patient the necessary information to lead him safely over a path which is never without danger is by no means easy. Enormous *tact* is required to prevent the *autosuggestion* which is harmful and which aggravates existing conditions. To absolutely ignore the dangers invites prompt death; to pilot with intelligence, with concert of action of the attendant and the patient often adds many years of life. What this means to mankind is apparent, when we consider the intelligence and the usefulness of those whom the disease attacks by predilection.

(*f*) *Senile Heart*

Balfour is probably responsible for the final acceptance of the "senile heart" as presenting a complex of symptoms which may justify the diagnosis. Senile heart is not a clinical entity. The symptoms depend upon degenerative changes in the cardiovascular system of the aged or prematurely old and include all of the usual clinical manifestations of such complex lesions with myocardial weakness in the ascendency. The prognosis depends upon the extent of the myocardial and arterial disorganization; it is always unfavorable, though the subjects of "senile heart" cautiously guarded, may live quietly during many months.

4. Hypertrophy and Dilatation

Hypertrophy and dilatation due to:

(*a*) *Overstrain*

Permanent or transitory dilatation and hypertrophy of the heart may follow severe strain, undue muscular exertion and prolonged worry. The possibility of preëxisting disease of the heart, or its muscle must always be considered. In the majority of these cases the history will prove that the heart was not normal before the strain.

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Undue strain long continued may certainly lead to hypertrophy.

In France the country letter carriers, who walk all day, suffer no ill effects from their long continued, and at times laborious marches, probably because *the normal heart, more than any other muscle, accommodates itself to its work.*

Rieder, Spillman, Bernheim, Thurn, assert that *with a healthy condition of the heart it is exceptional to find cardiac insufficiency and dilatation with consecutive hypertrophy following severe bodily exercise,* and most of these observers believe that the normal heart never tires, that in those who are perfectly healthy in spite of exhausting effort there is no typical cardiac insufficiency.

A full consideration of this subject leads us (Elsner) to the conclusion previously expressed. "It is safe and conservative to conclude, that the heart muscle, like all muscles, demands the natural stimulation which follows moderate functional activity and mechanical movements, but excessive functional activity, mechanical strain or prolonged mental pang and worry, cause malnutrition and irritation, giving rise to chronic degenerative changes" and may lead to hypertrophy and dilatation. This hypertrophy may take place in the perfectly healthy heart and is not to be considered pathologic.

In making *life insurance examinations* it should be remembered that *the hearts of young men and growing boys often show marked increase of systolic force and slight hypertrophy of the left ventricle. This is particularly true of the college student who is at all athletic, and should not argue against the acceptance of the risk.* These *hypertrophied hearts due to overwork which are to be included in the class of "work hypertrophies" never show degenerative changes if they were previously absolutely normal.*

The "overtrained" heart which was previously normal, which during periods of stress shows the effects on the cardiovascular system, after a time, varying in different cases, as a rule, returns to its normal condition and remains so. These experiences have been confirmed by many observers (Inndell).

(*b*) *Hypertension*

The influence of hypertension is considered with the separate conditions with which it is associated, and requires no repetition in this chapter.

I once more warn against misinterpretation of the prognostic value of blood pressure study, agree that long continued hypertension is a frequent cause of hypertrophy, that most of these cases are associated with established arteriosclerosis and renal involvement when detected, that its early detection and rational treatment often leads to satisfactory results, that in itself "raised blood pressure . . . . is productive of degenerative changes in the vessels" . . . Lauder Brunton further says "we have good

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grounds for believing that if the rise be detected early, and counterbalanced by proper regimen and treatment, the vascular changes which it would otherwise produce might be prevented and life very considerably prolonged."

(c) *Hypertrophy*

(Secondary to lung diseases, asthma, kyphosis, fixed thorax and non-valvular heart lesions)

The prognosis of the hypertrophy secondary to the diseases above mentioned requires no separate consideration, it must necessarily depend upon the seriousness of the underlying pathologic lesions. It is surprising to note the salutary *influence of hypertrophy on the general condition of these patients;* in most cases it may safely be considered compensatory and therefore favorable. *Extreme sudden dilatation occasionally causes sudden death or serious decompensation.*

Fixed thorax and some non-valvular diseases of the heart including hyperthyroidea with marked hypertrophy are often favorably influenced by surgical interference. This is true of the former (Starrer-Thorax), a fact not generally understood by the profession.

(d) *Hypertrophy*

(With masturbation, uterine-fibroids and hyperthyroidea)

With *masturbation* the heart is often irritable and overactive, the systolic force abnormally strong. These symptoms are associated with *moderate hypertrophy,* which yield with the dropping of the habit, and leaves no remnants.

Uterine growths are often associated with enlargement of the thyroid and other symptoms of hyperthyroidea and heart hypertrophy. I have called attention to this frequent association of uterine, thyroid and heart lesions in an article (Elsner) which proves this possibility and its unusual frequency.

All abdominal growths by pressure and added circulatory obstruction add to the work of the heart muscle. With uterine myofibromata of considerable size it is not surprising to find the myocardium insufficient without the loss of blood from flooding. The prognosis of the heart condition has been studied in the French hospitals, particularly by Pozzi, it is favorably influenced by surgical interference.

A small uterine polyp may cause heart symptoms, often continuous, and when persistent, hypertrophy may result; removal brings relief.

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5. Stokes-Adams Disease

(*Heart Block*)

The Stokes-Adams complex when fully established (See *also reference in this chapter to Irregularities due to depressed conductivity*) is an expression of advanced disease of the bundle of His making it impossible for impulses to reach the ventricle from the auricle; the ventricles and auricles beat independently of each other. *The phenomena of heart block include, bradycardia, epileptiform seizures, often syncope, visible auricular impulse in the neck, the rhythm usually 3 to 1, in all cases myocardial disease, often, positive evidences of arteriosclerosis.* The myocardial lesion always includes change of some kind in the auriculoventricular bundle (His fibers).

Lewis grouped his cases as follows showing the age distribution of Stokes-Adams disease:

Age.....	10–20	20–30	30–40	40–50	50–60	60–70	70–80	90–90
Cases.....	7	6	3	5	2	3	4	1

The symptom complex may occur at any age; the age distribution depends on the diseases which produce it.

The *rheumatic and choreic cases* include most cases between 10 and 35 years. The *specific and arteriosclerotic group* includes the cases between 35 and 70. *The senile group* includes a large number of cases with associated heart lesions.

Our series of cases shows the disease to be twice as frequent in men than in women.

Lewis calls attention to the *presence of heart block* with the acute infections in young subjects, particularly with *rheumatism, diphtheria, influenza, typhoid, and pneumonia.*

Our chronic cases have been either in the subjects of previous rheumatism, syphilis or with marked arteriosclerosis.

Heart block is often found during and after acute infections, or with valvular lesions in which large doses of digitalis have been responsible for the dissociation.

Heart block is always serious, it is in almost all cases the evidence of local disturbance which is a part of a widely disseminated process, just as a small placque over a coronary artery is a limited but fatal lesion of far-reaching arteriosclerosis.

Heart-block may be borne during long periods by some, but when the pulse falls to a very low level (15-25) *the epileptiform, at times apoplectiform state clouds the sensorium and death after convulsive movements*

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follows. The *larger number of deaths are due to the associated fibroid degeneration, uremia at times, cerebral apoplexy* and *sudden acute dilatation of the left ventricle.*

The mild rheumatic type and those cases of partial block associated with the acute infections entirely disappear during convalescence.

The specific cases offer a better prognosis when intensive treatment is instituted, than do the arteriosclerotic or fibroid types. I have in private and hospital practice seen encouraging results from the combined modern treatment (mercury and neosalvarsan) (Weintraud, Huchard, Barries).

Heart block, properly speaking, should include only those cases in which complete block does not exist; Stokes-Adams disease represents cases of complete block.

The occurrence of convulsions always increases the danger, though it must be conceded that they are more frequent with partial, than with complete block.

In my experience no patient has recovered in whom the underlying cause was of degenerative origin; the only recoveries included in the series were the syphilitic and those acute cases in young subjects, dependent on infection, rheumatism usually, pneumonia and influenza. Most acute infections which are sufficiently severe to include the complex, lead to death during the active days of the toxemia.

The longest *duration* of Stokes-Adams disease in my experience was in a man who for fifteen years had persistent bradycardia, his pulse beat was below the average of the respiratory frequency at all times, he had epileptiform seizures at varying intervals during three years before his death in coma. His age at death was 79.

I have had no experience with the so-called *"neurotic cases"* described by Edes and Councilman, which fail to show pathologic lesions on post mortem examination.

Death is usually sudden. Sapegno found lesions of the auriculoventricular fibers in 50 per cent of all sudden deaths.

Sternberg found some lesion of the bundle in 70 per cent of cases of all heart affections.

6. Syphilis of the Heart

See Cardiovascular Syphilis

7. Heart Weakness due to Insufficient Exercise

The myocardial weakness which results from insufficient exercise is often an accompaniment of long continued invalidism, or is due to other

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causes; at times the inertia of the patient and paralytic conditions make exercise impossible. The heart muscle may weaken in aged patients with fractures, usually of the hip joint. There may be alarming syncope when the patient first tries to change his position or stands, but the heart soon gathers strength and in the absence of organic change become normal.

8. Inherent Muscular Weakness

There are occasional cases of *inherent muscular weakness with an asthenic state, in which the myocardium promptly shows evidence of fatigue on slight cause.* Such hearts bear any added tax badly; the patient is without resistance and when overtaken by infection is unable to make the average fight against its advance. *Children who are constitutionally weak, in whom there is a distinct diathesis,* may be influenced by many factors to overcome the inherent weakness, which, when it persists, leads to an unhappy existence. I have found a number of these cases of inherent weakness among the intractable cases of *Akinesia algera* originally described by Moebius, which may lead to years of invalidism and which offer a doubtful prognosis (See Akinesia algera).

9. Insufficiencies with the Anemias, Metabolic Faults and Toxic States

Myocardial insufficiency is likely to develop with the advance of all of the graver anemias, with faulty metabolism and with many toxic conditions. The prognosis must depend entirely upon the character of the primary disease and cannot be separately considered.

10. Neoplasms

New *growths of the heart* are either *primary* or *secondary.* The *gumma* of specific origin is of greatest interest to the clinician; all other growths are interesting pathologically, but remain as a rule undiagnosticated during life.

The *primary growths* are:

Fibromata
Myxofibromata
Lipomata
Lymphangiomata
Cavernous myomata
Rhabdomyomata.

Myxomatous growths may form on the separate valves.

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The *secondary or metastatic growths* are:

Carcinomata (often from the esophagus)
Tubercle
Syphilitic gummata
Lymphadenomata
Extension of Hypernephromata
Sarcomata
Melanosarcomata
Xanthosarcomata
Osteosarcomata.

Direct invasion of the heart from the pericardium may follow *sarcoma of the thymus, cancer of the lung and pleura.*

Leukemic growths may also invade the myocardium.

The Stokes-Adams complex follows invasion of the intraventricular septum occasionally with neoplasms; with *syphilitic gummata,* this is comparatively frequent.

Some of the *innocent growths,* when small, may give rise to no symptoms during life, the malignant and semimalignant naturally hasten the death of the victim.

Tuberculosis and actinomycosis are separately considered.

11. Parasites of the Heart

The Echinococcus may find a resting place in the heart muscle (See Hydatid disease) usually in the right ventricle and unless of considerable size, causes no symptoms. When the *cyst ruptures, embolic infarcts* lead to death. These are found in the lung and distant organs.

The Cysticercus of the Tenia solium may settle in the myocardium. When symptoms are produced by the growing cyst, they never lead to a diagnosis. *Marked hypertrophy, dropsy and severe pectoral pains preceded death* in the few recorded cases. I have had no personal experience with either Echinococcus nor Cysticercus of the heart. We have found the heart infected with *Trichinae spiralis,* but their presence in the heart muscle as a rule does not materially influence the prognosis of trichinosis, so far as we know (See Trichinosis).

For a full consideration of the parasites of the heart the reader is referred to Mosler's articles. (See *reference.*)

12. Rupture of the Heart

I referred to rupture of the heart in connection with fatty heart and mentioned the fact that in 77 per cent of spontaneous ruptures Hamilton found fatty degeneration of the myocardium.

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13. Aneurism of the Heart

Aneurism of the heart is exceedingly rare; it is an occasional cause of rupture. It may accompany ulcerative malignant endocarditis and fibroid myocarditis.

Fibroid degeneration and the mixed forms of degeneration may also lead to aneurism and rupture.

Partial rupture may not prove immediately fatal. We found one case in which a partial rupture preceded death by a number of days, which was sudden and due to a second complete rupture. A *thrombus* may plug a small rent and prolong life during only a limited time.

Abscess of the heart wall may cause rupture—the majority of heart abscesses are micotic—are found with *malignant endocarditis, pyemic and septic conditions*—they may be *multiple* or *single.*

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F. Endocarditis

Endocarditis is either (1) acute or (2) chronic.

1. The varieties of Acute Endocarditis are:
   (a) Simple Acute Endocarditis (Thrombo-endocarditis simplex of Ziegler).
   (b) Septic Endocarditis.

   (Malignant or ulcerative endocarditis, Thrombo-endocarditis septica ulcerosa) (Aschoff)
2. The varieties of Chronic Endocarditis (Chronic Cardiopathy) are:
   (a) Valvular Deformities (resulting from previous Acute Endocarditis)
   (b) Degenerative Endocarditis (Arteriosclerosis—Syphilis)

Endocarditis is always of infectious origin, is secondary and not a disease per se.

To recognize its prognostic significance its pathology demands consideration. *The extent of the endocardium, the unevenness of its surface,* as well as *its irregularity, the mechanical factors continually present, invite the deposit and proliferation of bacteria.*

The endocardium offers a suitable and inviting culture medium, more particularly with changed conditions of the blood, and possible slight abnormality of the endocardial surface. This is especially true of the malignant, septic or ulcerative type of endocarditis.

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1. Acute Endocarditis

(a) *Simple Acute Endocarditis*

(Thrombo-endocarditis simplex of Ziegler, also known as Endocarditis verrucosa)

The prominent lesion of this form of endocarditis is the deposit of warty or papillary masses or bodies along the edges of the valves. The amount of deposit varies; it may be so insignificant as to escape the eye, or it may be prominent, forming masses of considerable size—uneven, irregular and of warty appearance. These masses on section show the character of thrombi, and hold within the included fibrin, platelets, lymphocytes with colonies of the infecting bacteria. There may be evidences of necrosis of the tissue of the endocardium or valve upon which the warty or papillary masses rest. *The extent of the necrosis is in direct proportion to the severity of the infection. The danger of embolic infarct increases with the extension of the necrosis and the loose attachment of the thrombi.* The replacing of the thrombi and of the underlying endocardium by connective tissue in the process of cure, including the valve structure, result in thickening, contraction, adhesions, leading to stenosis (narrowing) or insufficiencies in accordance with the extent of the original lesions. *Endocarditis may limit its ravages to the free surface of the endocardium without involving the valves.* This fact must be considered in the diagnosis and prognosis of infections in which unexplained symptoms of constitutional disturbance persist. The following figures show the relative frequency of the invasion of the valves:

The mitral valve is involved in 60 per cent; the aortic in about 9 per cent. The tricuspid and pulmonary rarely; the inflammation of both mitral and aortic valves is found in about 30 per cent of all cases. With simple endocarditis it is exceedingly rare to find the tricuspid inflamed with the mitral alone, or with the mitral and aortic valves combined. It is unusual to find all four valves attacked (Aschoff).

In simple endocarditis the bacterial invasion is not usually overpowering, there is limited loss of endocardial tissue, there may be none at all, the formation of emboli is infrequent—all these conditions prevail in the septic or malignant type of the disease—hence the prognosis so far as life is concerned, is good. Romberg denies the possibility of complete anatomic restitution after even simple acute endocarditis.

The extent of the damage done by an acute endocarditis cannot be foretold—this fact calls for a guarded prognosis concerning the future of the functional powers of the heart and at the same time suggests such prophylactic measures as should lead to the conservation of the organ. All forms of acute endocarditis are associated with more or less myocarditis,

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a further fact, which must be considered in connection with the primary disease during the period of endocardial involvement and the months following convalescence. *Pericarditis* (See Chapter Pericarditis) is also a frequent accompaniment of endocarditis; the significance of the former must be considered in connection with the degree of virulence of the primary infection and the extent of the endocarditis, as well as the character of the effusion. (See Pericarditis.) The mortality of the combined lesions reaches between 25 and 35 per cent.

All factors which overtax the heart during or after acute endocarditis invite permanent damage.

Endocarditis is subject to relapses; this is due to the tendency of polyarthritis to recur (the most frequent cause of the complication); and the further fact that the endocardium harbors bacteria in its folds and on its surface during long periods.

In the acute types, non-malignant, the left ventricle is usually the seat of the infection; with severer and ulcerative septic endocarditis, the right heart is frequently the seat of profound changes as well as the left ventricle.

I have considered the significance of endocarditis in connection with the many infections which it complicates and refer the reader to the separate chapters; they include *Polyarthritis, Scarlet fever, Tonsillitis, Typhoid fever, Pneumonia, Erysipelas, Diphtheria, Chorea, Syphilis, Tuberculosis, Gonorrhea, Pyemia, Sepsis, Nephritis, etc.*

With some forms of *grave anemia and cachexia,* endocarditis may develop and seriously complicate the prognosis. Probably some of these cases are of *toxic rather than of infectious origin.*

Endocarditis complicating gout, diabetes and *other constitutional diseases,* may, in the light of our present knowledge be included in the *"toxic type."* The prognosis with acute symptoms and material change in the heart muscle is to be guardedly given; all features of the case demand the closest consideration. These cases are not to be confounded with the endocarditis of degenerative (arteriosclerotic) origin which is frequent with faulty metabolism.

The Physical Signs.—In offering a prognosis, the clinician is not to interpret the loudness of the systolic murmur which is present and widely disseminated over the precordium in almost all cases, as indicative of a serious condition.

Let the greater reliance for prognosis be placed upon the virulence of the infection, the extent of the primary lesions, the general condition of the patient, the amount of dilatation of the heart, the character of the pulse, the functional ability of the kidney, the blood pressure, the size of the liver (enlarged in serious cases), the size of the spleen, the presence of infarcts, the blood picture and a variety of symptoms which are unearthed by close observation.

In children, while the prognosis is less favorable than in adults, in

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the absence of edema and in the presence of apparently serious endocarditis, recovery may follow with but limited damage to valvular structures.

Even with edema and multiple systolic murmurs in children and adults, recovery may follow with surprisingly insignificant damage in cautiously treated cases.

Loud and multiple murmurs with chorea, may disappear entirely, never to return, within a number of years. Return of chorea may in some cases remain uncomplicated, in others there are *acute exacerbations of endocarditis.* The prognosis of chorea with complicating endocarditis is not bad. In a large experience I have seen but two deaths; both children were enormously obese—in one the endocarditis was malignant.

With recurrences and extension, the damage resulting with increasing physical signs of myocardial insufficiency and dilatation, may lead to long periods of uncertainty, but in most cases life is saved; occasionally underlying conditions are serious, resistance is reduced and death cannot be averted.

Pulmonary edema, pneumonia, purulent pericarditis, thrombosis, embolism with hemorrhagic infarct and a mitral obstructive lesion are unfavorable complications, and include the most frequent causes of death.

Duration.—It is never possible to foretell the length of time during which the acute symptoms will continue; cases which often drag along during weeks and months without change in physical signs or subjective symptoms, gradually regain health with ultimate limited damage to the heart.

The previous condition of the heart is an important factor in prognosis. There is always danger of malignant endocarditis in cases of acute exacerbation of chronic heart lesions.

With early aortic insufficiency, the danger is greater than with the more frequent mitral insufficiency; the danger is greater with early mitral than with aortic obstruction.

The influence of age, sex, occupation and habits is considered with the resulting permanent valvular lesions. In all cases of simple acute endocarditis treatment, especially rest and right living enormously influences prognosis. *Many lives have been doomed to wretchedness and chronic invalidism by failure on the part of the physician, oftener the patient, to realize the great curative and prophylactic value of rest after acute endocarditis.*

(*b*) *Septic Endocarditis*

(Malignant, Infectious, Ulcerative Endocarditis; Thrombo-endocarditis septica s. ulcerosa—Aschoff)

In contradistinction to the superficial character of the lesions with simple acute thrombo-endocarditis, septic endocarditis shows deep invasion of valvular structures and of the free endocardium in a destructive,

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necrobiotic process; the formation of vegetations, abundant thrombotic deposit, and the presence of the virulent microörganism in great numbers. *Bacteremia* is present and can be demonstrated by blood-cultural methods in most cases.

Septic endocarditis should be considered to be of secondary origin in all cases; the exceptions are so rare as to require no consideration. There is no one pathogenic organism which causes the disease, it may follow in order of frequency *streptococcus, pneumococcus, staphylococcus, influenza bacillus, gonococcus infection* and in the *chronic forms of the disease the streptococcus viridans* (Schottmüller, Rosenow, Libman) is now established *as the leading factor, though there are many cases of chronic pneumococcus endocarditis and in all forms mixed infection may ultimately exist.* Aschoff suspects that the viridans is a modified pneumococcus.

The *avenues of entrance of the infecting agent* are numerous and often furnish surprises.

The blood is furnished with the specific organism from diseased tonsils, the lung, the genitalia (women oftener than men), *the puerperal uterus and adnexae, the bone marrow, the skin and from any source to which infection may be carried and from which the blood current is infected. Insignificant* (*apparently*) *traumatism* has in several of our cases led to malignant endocarditis. In two cases we found the passing of a urethral sound with slight bleeding followed by fatal endocarditis.

In the cases following the unnoticed and insignificant primary infection, the malignant nature of the endocarditis comes as a surprise. Often the primary disease is unheralded and overlooked—"In the endocarditis following the graver infections, one is dazed by the gravity of the primary malady and fails to look for secondary and malignant disturbances" (Elsner).

For prognostic purposes the frequency of septic endocarditis grafted or preceding valvular disease must be considered, the chronic lesion becomes an important and inviting factor. Goodhart showed that 61 of 69 cases presented old thickening of the valves, and mentions the occurrence of malignant endocarditis with aneurismal disease. He further says: "Patients with chronic sclerotic valves are walking mushroom beds, in common times without spawn, but in periods of epidemics germs enter by various channels, which fertilize in these cases into ulcerative endocarditis; in others to suppurative processes." Osler also mentions the frequency with which sclerotic disease of the aorta and valves is associated with malignant endocarditis. This is an exceedingly important fact for prognosis and with all primary infections, in the presence of chronic heart lesions it should not be ignored. Sir James Paget offered the data which proved the frequency with which changed valves suffer from acute disease. Of 84 cases of infectious endocarditis seen in St.

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Bartholomew's Hospital from January, 1890, to March, 1897, 51 were found in males, or 60.71 per cent, and 33 in females, or 39.29 per cent. The greatest number was found from the thirtieth to the fortieth years; most of the cases between twenty and forty. In these cases all but 10 were found either in patients suffering from old cardiac disease, or there was positive evidence of an infecting lesion. The tendency of old diseased valves in pneumonics to take on chronic malignant inflammation is surprising.

It has been established experimentally by Wyssokovititch, Oliver and Rosenow that infectious material introduced in the blood stream attacks by preference the valves and endocardium which have been traumatically robbed of their protecting endothelium. To Heiberg belongs the credit of establishing the fact that in these cases, the vegetations on the valves were bacterially contaminated. The complication of malignant endocarditis with septic conditions is fortunately comparatively rare, but with increased diagnostic skill it is more frequently found than formerly. Lenhartz found in the Hamburg Hospital 21 per cent of all general sepsis with endocarditis.

Romberg reports in 33,539 of internal diseases during 8 years, 243 cases of sepsis with 42 malignant endocarditides. In 6,670 cases of internal disease I found in my private and consultation practice 20 cases of malignant endocarditis including gonococcus and pneumococcus infection. Of 7,770 cases of internal disease among whites admitted to Johns Hopkins Hospital (1902-1911) there were 1,317 diseases of the circulatory organs, among these endocarditis was diagnosticated in 38 males with 21 deaths, 55.3 per cent, and in 12 females, 33.3 per cent. How many of these were malignant is not stated.

Endocarditis which is at first benign or appears to be so, may in the course of a few days end fatally with symptoms of malignant infection, while other cases which commenced with symptoms of malignancy may prove to be benign or non-septic.

It is exceedingly difficult in practice to draw a line which shall separate the severer benign, from the malignant types, either by clinical study or blood cultural methods during long periods in individual cases. Repeated negative cultures in cases of malignant endocarditis not infrequently leave the clinician uncertain as to diagnosis and prognosis during long periods. In some of these cases the involvement of the right heart argues in favor of malignant infection. Litten called attention to a variety of simple acute endocarditis associated with rheumatism which he styled "*Non-septic Malignant Rheumatic Endocarditis*," in which many cases prove unusually severe and often fatal. This type of endocarditis presents distinct features which must be considered separately and are not identical with those of malignant or septic endocarditis. In the favorable cases there is the same tendency to contraction and changes

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in the valves found in the less virulent forms. The right heart escapes involvement. *There may be infarcts and metastases but these are never malignant, there is greater tendency to pericardial involvement, and recurrences of acute exacerbations in those who recover are frequent.* There are no paralyses nor symptoms of embolism or purulent thromboses. Death usually results with cerebral symptoms; albuminuria is transitory, the spleen is less enlarged than in malignant endocarditis. In 209 cases of septic endocarditis, Osler reports the *tricuspid valve* involved in 19 cases; the pulmonary in 15; the *aortic and mitral together* in 41; the *aortic alone* in 53, the *mitral alone* in 77, *the heart wall* in 33, and in 9 cases he found the *right heart* involved alone. These figures prove the involvement of the right heart out of all proportion to the left sided disease in the less malignant or other forms of secondary endocarditis. The grave prognosis which is justified in all cases of malignant or septic endocarditis depends on the virulence of the primary infection, often mixed infection, the far-reaching local and general disturbances, the tendency of the diseased tissue to break down into minute particles which act as carriers of the infectious material to distant parts causing deep changes, hemorrhagic infarcts, mycotic aneurisms, and the further tendency to miliary abscesses, and purulent infarct in the various organs of the body, including the kidneys, spleen and heart. Harbitz and Libman claim that with the virulence of the infecting agent reduced, the local endocardial lesions may heal and cicatrice though the resulting damage to the valves and endocardium is greater than with single endocarditis. We have no case to report, in which if such healing process did occur the life of the patient was saved in our practice; in no case in which the diagnosis of septic endocarditis was positively established clinically and bacteriologically has recovery followed—this is the experience of nearly all clinicians. The following classification of Septic Endocarditis is most serviceable:

I. Intermittent of pyemic form.
II. Fulminating intermittent form.
III. Typhoid form.
IV. Cerebral form.
V. Chronic Cardiac form.

I. **Intermittent or Pyemic Form.**—Kirke and Traube dilated fully on the possibility of chills and fever and all of the symptoms of intermittent fever, with endocarditis. In these cases there is as a rule the history of preceding septic or purulent infection. Most cases are of *streptococcus origin*, show marked *leukocytosis, the spleen is enlarged; with delirium, rapid pulse, moderate albuminuria, occasional hematuria, positive physical signs, early changes in the quality of the heart sounds and equally early embolic infarcts, cutaneous and deep, they die.*

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In some of these cases where there are preëxisting heart lesions and consecutive murmurs, the character of these is often changed, and with this change there are transitory paralyses; sometimes evidences of embolic infarct in the skin, lung, brain, kidney or intestine, obstructive murmurs are often changed in character and occasionally become inaudible—for a time at least.

Intermittent types with puerperal phlebitis run a short course to a fatal termination. Petechiae are often abundant.

In these cases, as with all forms of septic endocarditis, the *endocardium may be plastered with granulations and deeply ulcerated without causing murmurs or other physical signs until within a few hours or days of death, or these may never appear.* The chronicity of some of these cases is striking. Some persist with final irregular intermittent fever during from four to six months. Most die within four to six weeks. The diagnosis of intermittent malarial fever has often been made in cases seen before the days of blood cultural tests; at present these errors are rare. Quinin is entirely without influence on the course of the disease. Most patients die with symptoms of cerebral infarct.

Among these intermittent cases, we recognize (a) *pyemic or septic form*, (b) *erratic intermittent form*, (c) *late cardiac intermittent form* and (d) *intermittent form with preëxisting heart lesions.* To the first of these,

(a) *Pyemic or septic form belong the cases of pyemia following puerperal fever.* These patients carry pus foci (one or more), may be about for a time, but the *course of the disease is usually short, always fatal.*

(b) The *erratic intermittent form may have erratic* chills, more or less continuous fever, the chills are very severe, the patient finally falls into a *typhoid condition* with a *zigzag temperature curve* during which the chills observe no periodicity, there is delirium, coma and death.

(c) *The late cardiac intermittent form* is characterized by *absence of positive physical signs during considerable periods, unexplained chills, fever and pyemic symptoms persist during several weeks when the objective features become clear and death follows.*

(d) *Intermittent form with preëxisting heart lesions* includes those cases upon which a malignant infection is grafted. This group of cases bears the strongest resemblance to malaria.

II. **Fulminating Intermittent Type.**—This type includes a number of cases which run a rapid course, terminating fatally in from ten to seventeen days, occasionally sooner.

Our series includes one case in which there was an infarct into the right eye causing complete blindness with characteristic quotidian fever and marked mitral systolic murmur. There were no petechiae. The source of infection remained undiscovered. The patient died before the

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end of the second week. Another death with fulminating intermittent symptoms was a child (obese) aged 12 years with violent chorea. There was, with the chills, hyperpyrexia, hematuria, cutaneous hemorrhages, delirium cordis, death in coma on the 13th day of the disease. Many of these cases show chronic endocardial lesions and they are likely to be of staphylococcus origin.

III. **Typhoid Form.**—The typhoid forms may persist as such from the beginning, or the typhoid state may precede or follow any of the other types. Most cases belong to this form. Pure intermittent cases often merge into a typhoid state and die in that condition.

Without chills, with more or less looseness of the bowels, enlargement of the spleen, leukocytosis (12,000-20,000), *increasing anemia, albuminuria, mental torpor with final cerebral infarct, in many, and with positive blood cultural finds, in almost all cases, these patients die in the course of from 6 to 12 weeks.*

IV. **Cerebral Form.**—Bramwell suggested the consideration of this type in his work on "Diseases of the Heart." *In all of these forms there is a strong tendency to coma and other cerebral symptoms as the disease advances. There is a strong resemblance to cerebrospinal meningitis* or *meningitis. In occasional cases there has been pneumococcus infection with pneumonia.* In two cases, convulsions preceded death. One of our cases was associated with purulent pericarditis. In some cases the vegetations were so placed as not to give rise to murmurs.

V. **Chronic Cardiac Type.**—This group includes all cases of chronic endocardial disease in which infection has led to mycotic endocarditis. The chronicity of these infections is characteristic with persisting bacteremia, *usually either pneumococcus or streptococcus viridans, erratic fever, anemia, leukocytosis, enlarged spleen, often joint pains, late in the course of the disease hematuria due to infarct, finally in most cases death from cerebral infarct or exhaustion. Septic Nephritis* develops in most cases. *In some there are mycotic aneurisms. Petechiae* are found in almost all cases at some time during the long duration of the disease. Some of our patients have lived from seven to thirteen months. Death is usually caused by one or more good sized infarcts. I have found the association of infarcts into the brain, lung, spleen and kidney. Occasionally one or more of the multiple infarcts are found sterile. *It may be assumed with considerable certainty, that the streptococcus viridans is the cause of most forms of chronic malignant endocarditis and that the prognosis is uniformly fatal.*

Gonococcus Endocarditis which should be included among the malignant types of endocarditis, offers only the most discouraging prognosis. It is fully considered in the chapter on gonococcemia.

The unfavorable prognosis which I offer in all cases of septic and gonococcus endocarditis is justified by my experience in spite of those

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cases in which from "time to time" greatly deformed cicatricial valves and remnants of infarct are found in patients who have died from other causes. Broadbent after mentioning these possibilities, concludes: "The number of authenticated cases recorded, however, in which recovery is reported to have taken place, is extremely limited, and it has not been my good fortune to see an undoubted case recover.

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2. Chronic Endocarditis

(*Cardiopathia chronica—Aschoff*)

General Considerations Included in the Prognosis of the Valvular Lesions of the Heart

Acute or recurring endocarditis leads to cicatricial changes in the valves of the heart making one or more of these insufficient or stenosed, causing consecutive changes in the heart and distant organs, in accordance with the character of the lesion.

There is, in truth, no true chronic endocarditis; the lesions produced are the results of gradual reparative changes which finally influence cardiac function and lead to the chronic endocardial and valvular defects above mentioned.

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The general acceptance of the term *"Cardiopathia chronica,"* offered by Aschoff is suggestive, and at the same time explanatory, and would do much to clear the horizon of the indefinite notions which are associated in the minds of many clinicians and students in connection with the misnomer "Chronic Endocarditis."

It is important to associate the chronic cardiopathies with two distinct primary processes, one inflammatory; the other degenerative. *The first, or inflammatory process*—is likely to attack the mitral valve by predilection and the neighboring endocardium; *the second, or degenerative process*—(*arteriosclerotic*) selects the aortic valve and the surrounding tissue, and often the aorta itself, is part of an existing general arteriosclerosis and is often associated with coronary disease and myocardial fibrosis.

With *mitral lesions* the degenerative or retrograde processes of the myocardium start in the coronary veins; with *aortic disease*, the lesions in the coronary arteries are likely to start the muscular insufficiency which is the threatening complication of all heart lesions. We are justified in considering the faulty compensation of *mitral disease* as a *"venous cirrhosis," that of aortic disease as "purely arterial."*

It is impossible to consider the diagnosis or prognosis of the cardiopathies (vascular lesions) without at once accenting the most important fact in cardiac pathology that *in the majority of cases murmurs give but little clue to existing dangers, that we find in the heart muscle "the key to the pathology of the heart"* (Stokes). Whatever the valvular lesion, "the symptoms depend mainly upon the strength or weakness, the irritability or paralysis, the normal or abnormal condition of the heart muscle."

It cannot be too often repeated that for safe prognosis we must assume that *valvular lesions per se, have but little influence on the general condition of the patient so long as the heart muscle remains healthy and sufficient.*

Gee's aphorism teaches a valuable lesson. "A beginner can hear murmurs and detect valvular disease, it requires long experience to appreciate nervous and muscular affections of the heart."

The seat and severity of the valvular defects naturally determine the secondary changes in the heart and other organs.

(a) **Hypertrophy.**—The heart learns to accommodate itself to changed conditions, it is built to bear insult, it is the most tolerant of all the necessary organs of the body.

With *stenosis* or *insufficiency* the heart undergoes such changes as are demanded by the increased tax made upon it. These must always be considered in connection with the separate valvular lesions. The general rule may be accepted without reservation, that whenever extra force and added energy are required, Nature makes a prompt attempt to develop the heart muscle to meet the demands; in other words the prognosis

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is influenced by the growth of the muscle, its increased strength, indeed the separate fibers show characteristic change (Tangl).

Only cases in which valvular lesions have existed a short time, fail to show some compensatory increase of strength. (*Hypertrophy.*)

For prognosis, the important factors to be considered are,

A. The reserve force of the heart.

B. Compensatory hypertrophy.

With the average defect, there is "a stasis behind the diseased valve and an anemia in front; the arteries consequently receive too little blood."

A. When called upon, the normal heart is competent to increase its force and strength of action thirteen fold (Zuntz).

The *reserve power of the heart* makes it possible for the organ when disturbed by a valvular lesion to prevent circulatory disturbances and embarrassment so long as the body is kept at rest, or the organ is not overtaxed, and the distant organs receive their quantum of blood and the arteriovenous balance remains undisturbed.

When extra work is thrown on the heart, the seat of any valvular lesion, the reserve is lowered.

B. Compensatory hypertrophy becomes an immediate necessity to equalize the circulation and to prolong life.

The demand which is made upon the heart to overcome an existing fault must determine the amount of necessary compensatory hypertrophy; under such conditions the prognosis is favorable in direct proportion to the ability of the heart muscle by increasing its volume, if conditions are continuous, to meet the added requirements. Under these conditions the prognosis is necessarily influenced by the ability of the patient to reduce the heart's labor, in other words, the subject of valvular disease if he fails to give the heart muscle the sleep or rest to which it is entitled adds an element which reacts unfavorably, for *the overtaxed and overtired muscle hypertrophies or compensates slower than does the muscle which has been subjected only to physiological strain.* The prognosis is further influenced by the spontaneity of the response of the muscle to react to the added task; the nature of the valvular lesion, the method of its onset and the other factors which influence the outcome of all heart lesions.

With *aortic obstruction,* the pressure within the left ventricle is increased during systole, the resistance offered by the narrowed or uneven ostium (valve) must be overcome and with *a favorably reacting left ventricle,* hypertrophy leads to sufficient strength to overcome the obstruction and the quantity of blood enters the aorta with sufficient force to meet all demands. These favorable conditions continue during many years in a large number of cases, are promptly influenced by conditions which increase obstruction in the periphery, by advancing degenerative

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changes in the arteries and increased blood pressure, by degeneration of the myocardium and other factors considered in connection with aortic obstruction and stenosis.

The prompt hypertrophy of the left ventricle which follows aortic stenosis is not characteristic of the behavior of the left auricle when the mitral valve is stenosed. Here the auricle because of its anatomic structure—poor muscular development—is less likely to hypertrophy, besides there are conditions in the pulmonary circuit which increase the amount of blood in the left auricle early during diastole, it is overtaxed during its systole, dilatation is invited and *the extra work then thrown upon the right ventricle leads to its hypertrophy.*

With moderate, almost insignificant mitral stenosis, a limited hypertrophy of the left auricle may prove sufficient to overcome the obstruction and the circulation may continue undisturbed.

With a high grade of mitral stenosis the pressure within the pulmonary circuit and in the left auricle is increased, and unless the hypertrophy of the right ventricle continues sufficient, a break follows which influences prognosis unfavorably. This condition is separately considered but it cannot be too often repeated that it is the leading danger of mitral stenosis.

With *valvular insufficiencies,* physical and mechanical conditions are different than with the stenoses. *In the former we are dealing with the regurgitation of blood into a cavity of the heart (with aortic disease into the left ventricle, with mitral insufficiency into the left auricle) and with both of these conditions the heart must of necessity contract with added strength to empty the respective cavity, but the cavity itself must accommodate itself to hold the surplus or extra blood which it receives.* More blood must be forced onward than the cavity normally receives during the period of rest. The result is change in the musculature to hold the extra blood and to force it onward.

In favorable cases compensation is synonymous with the increase of strength of the muscle and a sufficient degree of physiologic dilatation.

If dilatation is extreme, compensatory hypertrophy is less likely to prove prompt or satisfactory.

Extreme pathologic dilatation always retards or lowers the chances of the growth of the muscle fibers to meet the demands.

Regurgitant lesions (insufficiencies) tend to enlarge the openings situated behind the seat of the lesion. In most favorable cases in which the left side of the heart is enlarged, the right ventricle hypertrophies, thus maintaining the blood pressure in the pulmonary circuit.

(b) **Dilatation.**—The physiologic widening of a cavity of the heart to accommodate itself to a surplus of blood is compensatory as already suggested and with increase of systolic force conditions continue favorable.

If the heart muscle is weakened, the cavity is not entirely emptied;

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there is with increasing accumulation increase of dilatation and added demands are made upon the musculature of the organ. Unless this is successfully met, the stretching or dilatation of the heart may become extreme and evidences of such cardiac insufficiency are shown by added *dyspnea and physical signs.*

With aortic insufficiency there are two sources from which blood enters the left ventricle during diastole: the regurgitation from the aorta because the cusps are not completely closed, and the normal supply from the left auricle. The heart muscle is called upon to exert itself to empty the ventricle during systole of the added quantity of blood, besides the content which is normally present; sufficient force is demanded to send into the arterial tree all of the contained blood, besides contracting the ventricle to as nearly as possible its normal size. So long as this compensation continues undisturbed there is no fear of troublesome dilatation; when disturbed, the muscle lags behind, the blood accumulates in the ventricle, and pathologic dilatation without sufficient hypertrophy results.

The dilatation of the left ventricle which results from mitral insufficiency when associated with compensatory hypertrophy allows of sufficient discharge of blood into the aorta to compensate, without disturbing the circulatory balance.

Conditions.—The conditions which bring about the compensation necessary to insure a favorable prognosis with valvular insufficiencies are therefore a sufficient or physiologic dilatation to allow of the regurgitated blood and muscular strength to empty the chamber completely of its contents.

Blood Pressure.—When there is heightened blood pressure with insufficiency, dilatation becomes a serious condition and with the added systolic force needed to overcome the resistance in the periphery, there is, under failing conditions, an increase of residual blood in the ventricle, dilatation without hypertrophy and decompensation is the result.

With increasing dilatation of the left ventricle, relative mitral insufficiency may result; this in turn leads to dilatation of the left auricle and rise of pressure in the pulmonary circuit. The right ventricle is soon overtaxed in its attempt to overcome the resistance in the pulmonary artery, it dilates in unfavorable cases, tricuspid incompetence results with all of the secondary disturbances including dilatation of the right auricle and the evidences of stasis in the systemic veins and in the portal circuit. Under these conditions, the prognosis is exceedingly grave, the picture of circulatory embarrassment or break is complete.

Simple uncomplicated hypertrophy of the left ventricle is exceedingly rare. When present, without other physical signs it is due to arterial-aortic disease and often to some one of the *nephropathies.* With persistently high blood pressure the latter may be strongly suspected. Under

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these conditions with proper care, life may be prolonged during many years. (See Myocarditis, also Nephritis.)

(c) **Decompensation.**—The full compensation of a valvular defect may persist during many years and patients may die of intercurrent disease. In most cases of (valvular) defects, added work thrown upon the heart is promptly followed, even in the average unfavorable case, by some subjective or objective symptom of revolt.

In the majority of organic valvular lesions the heart tires ultimately and decompensation is more or less in evidence, in direct proportion to the weakness or lack of resistance of the myocardium.

In many cases the patient is responsible for the unfavorable condition because of overwork, excitement, excesses in diet, tobacco, coffee or alcohol, faulty living, exposure and a variety of depressing factors. Other agencies which invite decompensation are beyond the patient's control; they include acute infections and many other diseases (metabolic) recurring endocarditis, worry, pregnancy, traumatism, etc.

The myocardium always remains the prime factor in decompensation.

With aortic disease and increase of degenerative changes in the arterial tree (*arteriosclerosis*), the myocardium suffers and symptoms are increased; the forecast is made less favorable.

Increase of valvular changes (*contraction, insufficiency*) necessarily adds to the work of the muscle and calls for further compensation.

With valvular lesions the reserve force of the heart is reduced, the work which the organ accomplishes is often maximum or near the limit of its power, when this is exceeded, decompensation is likely to follow if the baneful factors persist.

In practice, it is never safe to assume, in spite of statements by excellent authorities to the contrary, that the hypertrophied heart is equal to the normal heart in its functional ability, that it is able to endure equal strain, that the reserve power of both is the same. *The safest rule to accept for prognosis is that the heart which is changed to compensate for an existing fault is never as dependable as is the normal heart, that to overtax such an organ adds an element of danger which may lead to irreparable damage and when the insult is persistent decompensation must be expected.* For the further study of hypertrophy, dilatation and decompensation and degenerative changes in the myocardium, associated with valvular lesions, the reader is referred to the chapter on Myocarditis and to the following works: Krehl and Romberg, Dehio, Stokes, Aschoff and Tawara and Gerhardt (See References at end of chapter). It is impossible to separate the study of the myocardium from the valvular lesion in prognosis, the latter is of secondary importance, a fact to which the clinician must cling at all times.

I have referred to increased blood pressure with arteriosclerosis as a cause of myocardial weakness and ultimate decompensation; in these

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cases the prognosis, even with included aortic valvular lesions is best in syphilitic arteritis.

Arteriosclerosis of the pulmonary artery or its branches with valvular lesions, aortic and mitral, in which the left ventricle is weakening, adds an element of danger and throws an added burden upon the right ventricle which may prove insufficient and lead to changes in the lung—bronchitis, pulmonary congestion or edema. Under these conditions the right ventricle is hypertrophied and insufficient.

The prognosis of dilatation of the right ventricle under all conditions is more favorable than is that of the left ventricle. The former may develop suddenly and promptly disappear, the latter is usually threatening and serious.

Hypertrophy of the right ventricle which continues during a considerable period is likely to prove permanent. On the other hand *dilatation of the left ventricle may yield to treatment,* there are many associated factors to be considered in making the forecast. *Acute, suddenly arising dilatation of the left ventricle is always of the gravest import.*

(d) **Frequency of Valvular Lesions.**—From three to five per cent of all internal diseases are due to chronic valvular lesions. Gerhardt gathered the following statistics showing the frequency of valvular disease. He found that in hospital practice from two to five per cent of all internal diseases were due to valvular anomalies. Leuch claimed 2.1 per cent, Schmidt 3.3 per cent, Guttman 5 per cent, Duchek 2.3 per cent, my own statistics 5 per cent (private practice). In private practice the number of heart lesions are greater than in most general hospitals. Gerhardt found that of 1,200 patients seen in private and consultation practice, 289 complained of heart symptoms with 65 valvular lesions, 115 myocardial disturbances, 109 neuroses. Of those complaining of heart symptoms 25 per cent have valvular lesions.

(e) **Sex.**—Sexes run nearly evenly with a small per cent in favor of the female.

The prognosis of heart lesions, i. e., valvular defects is more favorable in women than in men. This is true of all organic diseases of the heart, including its arterial supply.

Hoffman's statistics gathered at Johns Hopkins Hospital (1902-1911) show that of all forms of endocarditis 55.3 per cent of white males and only 33.3 per cent of white women died.

(f) **Heredity and Family History.**—Heredity has a powerful influence on the prognosis of the chronic cardiopathies; this is particularly true of lesions of the aortic valve. Schott found 26 per cent of all valvular lesions with a family tendency. *The prognosis is always less favorable with a clear family history of heart disease.* To this fact I refer in connection with angina pectoris.

With an aortic valvular lesion, the history of anginous attacks and an

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unfavorable family history the prognosis is correspondingly grave. Eichhorst and Mohr offer data which show positive hereditary tendency to valvular lesions in some families.

(g) **Age.**—Age is an important factor in the prognosis of chronic valvular lesions.

Young children with permanent valvular defects offer an unfavorable prognosis.

During the active years of life the prognosis of the lesions which result from inflammatory disease (mitral usually) is relatively favorable.

The *degenerative* (aortic lesions) *valvular lesions,* however, offer an uncertain and usually an unfavorable forecast.

Valvular lesions during old age are likely to be associated with such other senile defects as justify only clouded prognoses. With such patients arteriosclerosis is the most frequent accompaniment; the prognosis naturally depends upon the rate of its progression. In a large percentage of these cases the advance of the sclerosis is slow and not infrequently the process remains stationary during a number of years. Compensation for valvular faults in advanced life is often surprisingly prompt. The heart instead of undergoing atrophy is stimulated and enlarges. Leyden says, "the heart is the only organ the size of which increases during old age." He claims that the heart of the youth is "more likely to exhaust itself than is that of the older individual."

(h) **Occupation and Social Conditions.**—The influence of occupation and social status on the course of valvular lesions is of paramount importance. From the data given in the preceding paragraphs it is at once evident that occupations which require considerable physical effort, if continued, are less favorable than are those in which the patient is kept comparatively quiet.

Valvular diseases (*usually aortic*), in those who are subjected to *mental strain, worry, hurry and excitement* are not likely to hold their compensation. *Myocardial degeneration with aortic and coronary lesions and interstitial nephritis* (*sclerotic*) *are the complications which lead to death.*

The factors included in the stress of modern life lead many active business and professional men to an early fall in the presence of a chronic cardiopathy.

With mitral stenosis and aortic insufficiency the prognosis is often favorably influenced by occupation which conserves the patient's energies and strength and does not add a burden to the overworked heart.

The ability of the patient to control his movements, to take advantage of favorable climatic influences guided by intelligence and sobriety become enormous factors in his favor.

Though valvular lesions are usually incurable, patients are often responsive to intelligent supervision, and if their social status permits of

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the control indicated in the individual case with a healthy suggestion and sufficient optimism life is often made comfortable during many years.

(i) **The Influence of Intercurrent Diseases.**—Infections.—In spite of serious valvular lesions, the heart, under extra strain, in the presence of added disease, which in the perfectly healthy subject requires the assistance of a resistant organ, does its work satisfactorily and in the end the disease terminates favorably. The heart under such conditions bears the burden during the acute period of the complication, but there may be and often is a revolt during convalescence in some cases; with the disappearance of the acute symptoms the myocardium may be found weakened or degeneration may follow and insidiously undermine its strength. On the other hand, the heart may not be unfavorably affected, and after the added tax, the previous lesion is found unchanged.

Hearts, the seat of organic lesions with kidney complication, do not bear added infection well; this is especially true during the active years of life.

Old subjects with organic lesions of the valves, even aortic, bear acute non-malignant exacerbations fairly well provided the myocardium functionates normally; this is not true of aortic insufficiency or marked mitral stenosis.

The heart, the seat of a valvular defect with chronic infection superadded, bears the strain surprisingly well during weeks and months in the presence of high fever, rapid pulse and wasting disease. This is demonstrated by the chronicity of many infections of which tuberculosis, pyemia and viridans streptococcemia are examples. Some infections promptly establish cardiac tolerance, which for prognosis is of great importance, while with other toxic conditions the heart muscle seems without resistance and promptly wilts.

In the consideration of the infectious diseases we considered the chronic lesions which they complicate. A few general conclusions are here added to make reference easy and prompt. (The reader is also referred to the separate infections and their complications).

Pneumonia.—With aortic lesions and general arteriosclerosis in old individuals the prognosis in the presence of pneumococcemia is unfavorable.

All cases of pneumonia in subjects with valvular disease are grave, recovery is not impossible and takes place in a good number of cases.

Rolly and Blumstein report 1,048 pneumonics of which 17 had valvular lesions; of these 5 died—29.4 per cent against the average mortality of 21.6 per cent. A number of our cases made uninterrupted recoveries from pneumonia with chronic valvular defects of all kinds. The recovery is slow, the course of the disease is likely to be atypical, and the disease usually terminates by lysis.

Influenza does not influence valvular lesions favorably. *If pneumonia develops, the prognosis becomes grave.* The period of convalescence from

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uncomplicated influenza in the subjects of valvular disease is slow, and the heart continues irritable during long periods, the myocardium is often weakened and existing compensation is unfavorably influenced.

In influenza and pneumonia the prognosis depends largely on the degree of existing compensation and the general condition.

Erysipelas.—My experience with erysipelatous infection and chronic cardiopathies has been limited. Gerhardt reports that two of his patients made prompt recoveries. In both the lesions were old and well compensated with mitral stenosis and moderate aortic insufficiency. *With decompensation and erysipelas* the prognosis is unfavorable. In such patients, as Gerhardt says, the erysipelatous inflammation is likely to attack the edematous extremities.

Bronchitis involving the smaller tubes with advanced valvular disease may lead to sudden death or to serious symptoms which often continue threatening during many days.

Bronchiolitis and bronchopneumonia in young subjects and in the aged are always serious and are among the most frequent causes of death of old subjects in hospitals.

Recurring tonsillitis in young subjects is a frequent cause of acute exacerbations of chronic cardiopathies and increases all factors which lead to greater permanent damage than previously existed.

Malignant Endocarditis.—The dangers of malignant endocarditis as a complication of chronic valvular disease has been separately considered in this chapter. (See Septic or Malignant Endocarditis.)

(j) **The Influence of Marriage and Pregnancy on Valvular Disease.**—My personal experience with the results of pregnancy on the subjects of valvular disease has been surprisingly favorable. In an active practice of over thirty-seven years I recall but three deaths of patients with valvular disease during pregnancy, or as the result of childbirth. There is, however, a great difference of opinion in the profession as to the influence of marriage and pregnancy in women with chronic valvular lesions and as to the advisability of recommending marriage to them.

The variation in the statistics of observers in the mortality of heart lesions during labor is shown by the following percentages of death:

Mueller	3.0	per cent.
Gusserow	6.0	" "
Wiesenschal	12.5	" "
Lewoff	12.0	" "
Jess	31.5	" "
Guerard	34.0	" "
Schalyer	48.0	" "
Wessner	49.3	" "
Von Leyden	55.0	" "
Lublinsky	60.0	" "
MacDonald	61.0	" "

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Fellner's statistics prove two important prognostic facts. One, that the percentage of reported cases was much too low and did not include many with organic diseases of the heart, which were discovered on careful routine examination; (it was found that six of seven cases of compensated heart diseases were escaping the attention of the examiners at the clinics) and the other was the cautious treatment and watching of these cases which lead to the advice at the Schauta Clinic to "terminate pregnancy in cases of mitral stenosis as soon as the slightest signs of broken compensation appear" or whenever evidences of danger were present in previous pregnancies. (Hirschfelder.) There was but one death in twenty-one pregnancies complicated with valvular lesions at the Schauta Clinic. In ten years Fellner found 81 cases, in which three mothers were lost and 26 children. The highest mortality was found in mitral uncompensated stenosis among the newborn. Seventeen mothers with one death, ten children died. Among 900 pregnant women there were twenty with valvular lesions, one death and five children lost. The one death was in a case of mitral stenosis uncomplicated. Hirschfelder says:

"These statistics from unselected cases are much more favorable than the previous reports would indicate, and are in accordance with the conclusions of Hicks and French that few women with heart disease are sterile, that they are not particularly liable to abort and that most of them bear children well."

Occasionally sudden death takes place before labor during advanced pregnancy, of chronic mitral insufficiency, broken compensation and renal invasion. I have seen cases in which, without the approach of labor, and evidently no factor added save the changes which accompany pregnancy, after a few days of increased dyspnea, death followed suddenly from acute dilatation.

Relative tricuspid insufficiency persisting during pregnancy or organic insufficiency with increasing dyspnea and cyanosis, enlargement of the liver, with or without edema of the extremities is a serious condition, and may in the pregnant woman lead to death at the time of labor or before. Much will depend on the care of these cases. I have recently seen such a case which we referred to a young and conscientious obstetrician, in which all symptoms seemed unfavorable, but which with persistent attention to detail, in a well appointed hospital was carried safely through labor and is still living.

The persistence during pregnancy or labor of the usual severe symptoms of broken compensation with any chronic valvular lesion is of serious import.

With dyspnea, orthopnea, cyanosis and albuminuria and an uncompensated valvular lesion, women rarely live long beyond labor. Hirschfelder says, "in from 25 to 40 per cent of patients with severe heart lesions the pregnancy does not reach term, but premature labor occurs spontaneously

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owing to partial asphyxia of the fetus." These statistics, so far as the premature expulsion of the fetus are concerned, are much higher than any which we have been able to gather in our own practice or from our colleagues. The statistics of mitral stenosis give a higher mortality for mother and child and approach those of Hirschfelder. Abortion is also more frequent in these. Fellner found 26 per cent of stillbirths among women with valvular lesions. Occasionally *aortic lesions* which are very rare during the child bearing period *cause sudden death.*

Mackenzie holds that dilatation during pregnancy affects the right heart, and that a woman otherwise normal may develop a definite tricuspid insufficiency as shown by the presence of a systolic murmur in the tricuspid area and venous pulse. This murmur may come and go, returning under varying conditions of the patient, it is therefore a relative insufficiency. These hearts may break compensation and pulmonary edema develops. This is most likely to happen with added *mitral stenosis and pulmonary engorgement preceding.*

Slemon and Goldsborough and Williams and Slemon have studied the *influence of labor on the heart* and they report that *the act of labor itself does not add to the strain of the heart unfavorably.* This is certainly true of a heart with a good myocardium.

With marked or limited myocardial degeneration of whatever nature, with or without valvular lesions the added strain of pregnancy and labor is likely to lead to a very serious condition in which the life of both the mother and the fetus are jeopardized.

If there is any one condition which justifies the interdiction of marriage it is valvular disease with persistent myocardial insufficiency.

Marriage is not without its dangers to the woman who has a valvular defect. The question which presents to the physician—whether marriage is to be sanctioned—can only be answered by a painstaking survey of the individual case.

In the presence of a well compensated heart, with mitral insufficiency or moderate aortic obstruction or a combination of valvular lesions which are well borne, in the absence of other defects, with a normal urine and favorable surroundings, marriage may be sanctioned.

With aortic insufficiency and with mitral stenosis both marked, with consecutive changes, there is just reason for hesitation. Marked hypertrophy and moderate dilatation with the former, in our opinion is sufficient to interdict marriage. Moderate mitral stenosis with compensation may under favorable conditions justify marriage, but an advanced degree of stenosis with secondary changes in the right heart does not justify the clinician, who must assume the enormous responsibility of deciding the question to recommend marriage. The same holds true of the advisability of the marriage of a man who has similar valvular defects and secondary changes.

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The social status with all that is included in environment becomes an important factor in deciding upon the future life of the woman as well as of the man in the presence of valvular and myocardial disease.

(k) **Influence of the Usual Complicating Diseases on the Course of the Chronic Cardiopathies.**—*Pericarditis* is separately considered (See Pericarditis) as a frequent complication of all forms of endocarditis.

There are occasionally acute forms of pericarditis which complicate chronic valvular lesions and arise suddenly; many of these are of the dry type (pericarditis sicca), others accompany acute exacerbations of rheumatic origin. Unless there is considerable effusion or purulent pericarditis, the addition of dry pericarditis does not affect the chronic cardiopathy unfavorably. *With added septic infection and pericardial invasion the prognosis is always bad.*

Diseases of the Respiratory Organs.—*Persistent disturbances—bronchitis and pulmonary stasis* are found in the more serious cases and terminal stages of valvular disease, they influence prognosis unfavorably.

Degenerative changes in the endocardium (arteriosclerosis) *myocardial fibrosis and chronic bronchitis* proves a complex which is rebellious to treatment, is occasionally favorably influenced by climatic change, but allows of only the gravest forecast.

Cardiac Asthma and Dyspnea.—For prognosis, in the presence of a valvular lesion, a prompt test of the resistance of the heart can be made by cautiously leading the patient to exercise and noting the result on respiration and pulse. *Dyspnea* on slight exertion is evidence of insufficiency and gives the safest indications for treatment and prognosis which we possess. *Relative muscular insufficiencies* are thereby developed which are also significant.

Severe dyspnea and cardiac asthma appear threatening at times, but under treatment in many instances disappear even in the presence of dropsies and other symptoms of insufficiency. The prognosis should in the average case be made only after the trial of rational treatment and rest. In these cases, particularly with mitral insufficiency, results are surprising and improvement is held during long periods.

With hydrothorax, hydropericardium, dilated left ventricle and an insufficient right heart and general anasarca the prognosis is grave.

With aortic lesions and cardiac asthma and dsypnea, the prognosis is less favorable than with mitral insufficiency. With aortic lesions and coronary sclerosis, cardiac asthma, with or without stenocardia, the chances for the patient to lift himself out of the attack are much reduced, though the heart may mend during considerable periods under such unfavorable conditions.

Dyspnea and cardiac asthma depending on auricular insufficiency are more favorable than are similar symptoms with ventricular disease (dilatation, etc.).

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Cardiac asthma with pulmonary edema when a sudden complication makes the presage unfavorable in almost all cases.

Brown Induration of the Lung.—Brown induration of the lung is always proof of long continued insufficiency. The weakness and dilatation of the left ventricle with bronchiolitis and the characteristic "cells of heart failure" in the sputum must lead to a guarded, usually unfavorable prognosis. In these cases of bronchitis due to brown induration, and congestion or edema, the sputum is rich in albumin in contradistinction to the sputum of uncomplicated bronchitis. (The Fr. v. Mueller test aids in diagnosis and prognosis. Add to the sputum three times its volume of a three per cent acetic acid solution, shake thoroughly and filter; then add a few drops of ferrocyanid of potassium solution when the albumin content will be precipitated).

Pulmonary edema due to dilatation of the left ventricle is more serious than stasis caused by right heart change. The latter is often of short duration, the former in the presence of marked valvular insufficiencies and organic muscle change frequently leads to prompt death.

The significance of hemoptysis depends entirely upon its cause. There are cases of moderate stenosis of the mitral valve in which hemoptysis continues during long periods without seeming to have any unfavorable influence. The bronchial or pulmonary hemorrhages are not as a rule threatening or profuse. Aortic lesions rarely lead to hemoptysis.

In occasional cases of mitral stenosis, tuberculosis may prove to be the cause of hemoptysis.

With congenital or acquired pulmonary stenosis, tuberculosis is frequent and the bleeding is a symptom of ulcerative or disorganizing change.

Embolic infarct may be a cause of hemoptysis; when present with the exacerbation of a chronic endocarditis it is of malignant or septic origin and offers an unfavorable prognosis. Infarcts also accompany non-malignant valvular lesions and are always to be interpreted as being of serious moment. They are found in the lungs of patients who during considerable periods had broken compensation. *Pulmonary infarcts* usually lead to death within a limited period because they are in the majority of cases coincident with fully developed cardiac asthenia; an occasional infarct may not be followed by death, recovery may slowly follow and compensation restored. Ginsburg presents interesting data. Of 250 autopsies in subjects who died of heart diseases there were 197 with valvular lesions; of these 85, 34 per cent showed emboli, 35.4 per cent had endocarditis of the left ventricle, 47.1 per cent of both ventricles, 29.4 per cent myocarditis, 20 per cent dilatation and hypertrophy. Infarcts were found in the kidney in 62 cases, spleen 23, brain 15, lungs 14, intestinal mucosa 3, tibial, bronchial, brachial, coronary arteries each once and once each in the pia mater and uterus.

Tuberculosis.—The association of tuberculosis and chronic valvular

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lesions is considered in the chapter on tuberculosis (Cardiovascular Tuberculosis). *Congenital pulmonary stenosis, mitral and aortic stenosis are often found with lung tuberculosis.*

Pleurisy.—Pleurisy may complicate valvular lesions, is often present with pulmonary infarct; if the effusion is small it does not influence the case unfavorably, if large it adds to the danger.

Most pleural accumulations are non-inflammatory and are the direct result of cardiac insufficiency. (See Hydrothorax and the separate Valvular Lesions.)

(l) **Blood.**—When with advanced valvular lesions there is *polycythemia,* it is an indication of insufficient heart strength and imperfect oxygenation. The loss of the watery element of the blood with extreme concentration in the terminal stages with dropsies is unfavorable and death under these conditions is not long postponed. With insufficiency of the right heart, cyanosis and polycythemia are often long tolerated and may yield to treatment.

Increased viscosity of the blood is found in cyanosed patients and with extreme insufficiency—evidence of extreme danger.

Various grades of *anemia* are found during the course of most valvular lesions at different times, their prognostic significance depends upon the underlying condition rather than on the blood state.

(m) **Skin.**—The skin shows changes which the experienced clinician interprets at a glance in many cases. The mottling and cyanosis, the cold extremities, the clubbed fingers and the evidences of chronic stasis with dermatitis or eczema are among these.

(n) **Nephritis.**—True nephritis is only rarely an accompaniment of valvular disease. Chronic congested or cyanosed kidney including the accompanying albuminuria is a frequent expression of stasis and muscular insufficiency. *Infarcts into the kidney* are frequent with malignant and benign endocarditis. These give rise to so-called *hemorrhagic nephritis.*

Chronic Interstitial Nephritis or the *arteriosclerotic kidney* (See Chronic Interstitial Nephritis) with aortic lesions and general arteriosclerosis deserve separate consideration and is part of a general process. When present with any form of valvular disease it adds to the dangers and influences the course of the disease.

(o) **Liver.**—*Enlargement of the liver, acute or chronic,* with valvular disease is a frequent complication, and is often an expression of insufficiency of the right ventricle, is present in mitral disease with decompensation. Advanced stasis, the cause of liver enlargement in these cases leads to *ascites, gastritis, enlarged spleen and many depleting intestinal symptoms. Organic change may lead to cirrhosis.* (See Pericardial Pseudocirrhosis).

Tricuspid insufficiency is a frequent cause of liver enlargement. *Jaun-*

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dice, when persistent or with cyanosis and other symptoms of stasis has in our experience proved to be of serious significance. It is not infrequent in cases of malignant endocarditis, grafted on chronic valvular lesions.

Gall-stone colic may lead to sudden death in the presence of a thin heart muscle and valvular disease. We include one such case in which an obese woman with chronic mitral obstruction and fatty heart died during a gall-stone colic of rupture of the left ventricle.

Frequent exacerbations of cholangitis and cholecystitis with gall-stone disease and valvular defects may lead to acute infection of the diseased endocardium, malignant endocarditis and death. Naunyn, Lenhartz and Elsner call attention to these cases.

(p) **Nervous System.**—Psychic Disturbances.—Psychoses are relatively frequent with valvular lesions. Kraepelin believes that venous stasis accounts for most of these. Romberg found thirteen psychoses among 1,200 heart diseases, mainly of the depressive forms.

Complications.—Epilepsy, hysteria, neurasthenia, persistent insomnia, somnolence, involvement of the respiratory center, Cheyne-Stokes breathing, persistent headaches, vertigo, chorea, and anomalous sweating are among the many complications referable to the nervous system. All of these conditions, particularly the psychoses, epilepsy, hysteria and neurasthenia, may develop without in any way influencing the valvular lesions; the psychoses themselves offer a less favorable prognosis with chronic valvular lesions than do those which complicate rheumatic acute endocarditis.

(q) **Dropsies.**—To these the author has referred in considering the prognostic value of other symptoms and in connection with the dangers of the separate valvular lesions.

(r) **Pulse.**—In considering the pulse we are again reminded of the fact that whatever prognostic data we obtain from its study must be furnished by the myocardium, upon its efficiency, its ability to overcome and accommodate itself to existing faults, clearly demonstrated by modern methods of examination depends the future of the patient. The pulse is fully considered in connection with the lesions of the individual valves and with myocarditis.

(s) **Blood Pressure.**—(See Consideration of the Lesions of the Individual Valves.)

(t) **Röntgen Examination.**—The use of the x-ray for purposes of diagnosis and prognosis has become invaluable in practice. By the aid of the fluoroscope and the Röntgen photogram we are at once, in most cases, given a view of the size of the heart, more particularly the left ventricle and the right auricle and the relation of the organ to its surroundings. These results can be corroborated by the orthodiagram. *Repeated x-ray examinations permit of the close observation of the effect of treatment and its influence on the organ.* The changes which follow in the blood

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vessels closely related to the heart and in distant organs which influence the course of valvular lesions are easily followed. For a full study of this subject the reader is referred to the splendid works of Groedel and Schwarz. To gain valuable data for prognosis, the examinations should always be made by those who devote themselves to this special work. *Interpretation demands experience.*

(u) **Sudden Death and Valvular Anomalies.**—Sudden death is an exceedingly rare occurrence with chronic valvular disease of the heart. There are warnings in almost all cases given by the failing muscle and the increase of secondary manifestations. The heart may occasionally, as in aortic insufficiency with dilatation and faulty compensation, stop without warning, but such sudden end is exceptional.

With an unchanged or compensated muscle the heart will continue the struggle; under such conditions there is sufficient reserve force to prevent stasis and sudden acute dilatation. When there is increasing secondary engorgement and the reserve is insufficient, the abundant symptoms and physical signs give timely warnings.

Aortic lesions associated with coronary disease (angina pectoris) may lead to sudden death. Such patients stand on the edge of a precipice, they may fall at any time. Under control, women particularly, may live during long periods. Less than two per cent of mitral lesions lead to sudden death. (Leyden.)

Obese patients—large portly men—with small fatty hearts, weak and rapid pulse, with arteriosclerosis and aortic stenosis (degenerative) are always threatened and often die suddenly.

(v) **Anatomic Cure of Valvular Lesions.**—Unquestionably there are cases of acute endocarditis which are followed by well marked physical signs of valvular deformity, murmurs, and muscular changes, in which all physical and subjective symptoms disappear and the patients continue well.

Post mortem examinations prove the possibility of the complete anatomic cure of valvular lesions.

Mitral insufficiencies of organic origin have disappeared, never to recur. (*Amsler, Leyden.*) The clinician should assure himself that he is not dealing with relative insufficiencies in these cases.

(w) **The Influence of Treatment on Prognosis.**—With full compensation, well regulated life, quiet temperament and a healthy suggestion which allows the heart to remain light while the brain is agreeably occupied, many patients with valvular lesions live in comfort during many years.

The *psychic element* in all forms of heart lesions is overpowering, it influences longevity materially for good or ill. The physician is largely responsible through his personality and included tact for the creation of a healthy optimism which means so much to the patient.

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The influence of rest, well chosen and properly directed baths and exercises is often paramount in the presence of the waning heart muscle.

The reaction of properly selected cases to digitalis is of enormous value in piercing the future of the cardiopath. Prompt reaction to digitalis in the presence of mitral disease is always encouraging. The prognosis is best in those cases in which the favorable effect of the remedy continues during a comparatively long period. When the effect is evanescent or of short duration, and the remedy is necessarily required at correspondingly short intervals there is danger that it may soon fail to produce the satisfactory strengthening of systole. Naturally the prognosis depends upon the ability of the therapeutist to administer the remedy *secundum artem* and upon the continuous supervision of the life of his patient.

There are cases in which *dropsies with incomplete compensation* and threatening symptoms due to distant stasis yield and under rational treatment such patients may live during many years.

The *specific* (*syphilitic*) *lesions of the valves, usually the aortic,* offer favorable prognosis in direct proportion to the improvement which follows modern treatment. (See Cardiac Syphilis.) The prognosis of heart lesions has been enormously influenced by the indications for treatment suggested by the Wassermann reaction of the blood in the larger number of aortic lesions.

(x) **The Influence of Physical Signs.**—The prognostic significance of physical signs is readily shown by the relative dangers of the different valvular lesions to which reference is made in considering these.

The fact which should be forcibly impressed upon the beginner is that *loudness of the murmur as a rule, bears no relation to the gravity of the lesion. It is often more favorable than soft or low murmurs.*

Systolic murmurs are more favorable than are the diastolic; in many cases they finally prove to be of functional origin (hemic, etc.). Naturally in offering the forecast, attention must be given to all of the many details considered in this chapter.

Diastolic and presystolic murmurs are almost always of organic origin and demand serious thought and attention for prognosis.

The *abnormalities of rhythm—intermission and arhythmia*—are considered with the separate lesions and in the chapter on myocarditis.

Delirious hearts (*delirium cordis*) are often well borne. They always add to the danger. When due to *auricular fibrillation* the prognosis is much better than with the ventricular disturbance; *alternating pulse with any form of arhythmia or myocardial disturbance is unfavorable.*

(y) **The Fate of the Chronic Cardiopathies.**—Romberg found that the duration of the period of compensation averaged seven years. One-third of his cases went beyond that time without a break, and the maximum period was found to be thirty-eight years; one-third of his cases remained without compensation from the beginning.

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Gerhardt reports 300 cases of which 123 allowed positive conclusions:

Duration of Compensation.	No. of Cases.	
0– 5 years	37	The average was twelve years.
6–10 years	33	
11–20 years	30	
21–30 years	9	
31–40 years	12	
41–44 years	2	

The average duration of primary compensation in man is nine years, in woman ten years (Gerhardt).

Localization of Valvular Lesions and their Forms

The prognosis of chronic valvular disease largely depends upon the valve affected and the degree of resulting deformity. There is an enormous difference as has already been hinted in the dangers of mitral and aortic disease. Most authorities claim that aortic insufficiency is the most serious of all valvular lesions, including Osler, while a large number including Colbeck and Gerhardt claim that mitral stenosis is the most serious. Osler calls attention to the fact that, in women particularly, mitral stenosis is almost on a level with mitral insufficiency. *Uncomplicated aortic stenosis* is the most favorable of all lesions, *mitral insufficiency* when well compensated offers a good prognosis.

Aortic stenosis and mitral insufficiency are the most frequent valvular lesions after the thirtieth year.

Mitral Insufficiency.—Over 50 per cent of all valvular lesions are due to mitral insufficiency. Mitral insufficiencies both alone and associated with other valvular lesions were present in 64 per cent of the Johns Hopkins Hospital cases, occurring alone in 29 per cent.

Mitral insufficiency offers greater encouragement for complete anatomic cure and insures longer periods of compensation than does any other valvular lesion. With *mitral insufficiency* the following facts require consideration in offering a forecast besides those included in "General Considerations of the Valvular Lesions."

The cause of the lesion bears directly on prognosis. Rheumatism, chorea and scarlet fever justify the most hopeful outlook, because in the large proportion of cases there is no danger of exacerbation after reasonable immunity.

Full compensation may never be disturbed, the future is often in the hands of the patient. *Reasonable care insures safety in most cases.*

Mitral regurgitant murmurs due to chorea disappear after a few years. Sir Andrew Clark taught that they never were found after ten years.

Mitral insufficiency is more amenable to treatment than any of the other valvular lesions.

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Dropsies which have existed only a short time with mitral insufficiency and without extreme loss of compensation often yield, and life may continue many years. *Extensive dropsies* always add to cardiac embarrassment. Mitral insufficiency with long continued dropsy and evidences of broken compensation justify a guarded prognosis, the result of treatment must clear the horizon. Associated conditions bear directly on the outlook.

With mitral insufficiency, "arteriosclerosis-insuffisance mitral-arterielle" of Huchard—which is usually caused by gout, lead poisoning, or dietetic excesses, is frequently associated with renal disease," and dyspnea is often severe and prognosis grave (Moon).

With arteriosclerotic changes in the endocardium, there is tendency to progression and a less favorable outlook than with the "endocarditic form of valvular disease."

Blood Pressure.—Much depends on the resistance in the peripheral vessels. With abnormally heightened blood pressure the force of the regurgitation is increased, the backward pressure in the left auricle is augmented and an added demand is made on the right ventricle.

Pulse Pressure (amplitude) is far more reliable than simple systolic blood pressure, for it gives an index of the burden which the heart is carrying. Undue frequency of the pulse with arhythmia perpetua due to *auricular fibrillation* need not always to be seriously interpreted. Digitalis will usually control the symptom. The *perpetual arhythmia* is less significant with mitral disease than with aortic.

When in mitral insufficiency the heart which has been regular and its frequency within reasonable limits suddenly develops perpetual arhythmia it signifies increased weakness or dilatation of the left auricle and nothing more, but this fact must be added to the many details of the individual case if safe conclusions for prognosis are to be reached.

Decided fall of blood pressure (hypotension) is unfavorable; it usually signifies myocardial insufficiency.

In all cases of mitral insufficiency physical signs should be watched for evidences of dilatation (increase in the transverse diameter) and evidences of stasis.

The pulse is increased in size so long as compensation is sufficient, therefore a favorable sign.

A small, thin, rapid pulse ("mitralized pulse") is proof of insufficient muscle strength.

Pulmonary stasis and dyspnea go hand in hand; they indicate broken compensation. The strength of the left ventricle is of greater prognostic value in considering pulmonary stasis than is that of the right ventricle, for the former when acting well empties its own cavity of more blood than the right ventricle pumps into the pulmonary artery. There is

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therefore a surplus of blood leaving the lungs under these conditions until the congestion is relieved.

Hirschfelder says, "The whole condition may be summed up by the statement that a weakly acting left ventricle overfills the lungs with blood, while a strongly acting left ventricle bails them out. The whole of pulmonary engorgement is, as rightly claimed by V. Basch, a problem not of the right ventricle, but of the left."

Accentuation of the second pulmonic sound indicates involvement of the pulmonary circuit, this is not always significant. Mitral insufficiency may continue during years with an accented second pulmonic sound with good compensation without the addition of serious complications. The following summary may be safely followed:

The favorable cases of mitral insufficiency are those in which compensation is sufficient; there is no dyspnea, no dropsies, the pulse is full, not excessively rapid, pulse pressure within normal limits, general condition satisfactory, urine free and non-albuminous, no enlargement of liver or spleen, and physical signs correspondingly encouraging, including moderate enlargement of the left and right sides of the heart; the second pulmonic moderately accented.

The *unfavorable cases* are those in which the leakage is large, pulse is "mitralized"—weak, rapid, irregular, pulse pressure and blood pressure are reduced, heart cavities dilated, the right ventricle particularly, and the left insufficiently hypertrophied; the murmur obliterates the first sound of the heart entirely, the second pulmonic is greatly accented, the radial artery cannot be felt between the beats, there is continuous dyspnea and evidences of pulmonic and systemic engorgement."

Lung complications—pulmonary edema, pleurisy with effusion add to the work of the heart, overtax the right ventricle and cloud the prognosis. For the significance of embolic infarct, thrombosis, pericarditis and other complications, the reader is referred to the General Considerations, etc., of Valvular Lesions.

Mitral Stenosis.—The outlook is influenced by the degree of mitral obstruction.

Moderate stenosis is tolerated during many years, in fact during a long and comfortable life without causing subjective symptoms and is often accidentally discovered post mortem.

Extreme stenosis leads to secondary changes because insufficient blood is forced into the left ventricle, the arterial tree is correspondingly empty, there is stasis in the left auricle, the pulmonary circuit, and the right ventricle is called upon to overcome the obstruction by added muscular force, *hypertrophy and dilatation result.* When the right ventricle is overtired and overtaxed, dilatation increases, the reserve muscular force is exhausted and decompensation with all of its complications is in evidence.

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Mitral stenosis almost always includes a degree of insufficiency, it is not infrequently associated with aortic insufficiency also. The majority of mitral stenoses are moderately developed or mild.

With proper rest and cautious living and without added burden thrown upon the heart such cases live in comfort during many years, barring complications.

Unfavorable Features.—Unfavorable features are increase of dilatation of the left ventricle, thrombosis and embolism, increasing arterial anemia, added pulmonary complications including cardiac asthma and dyspnea, edema, hydrothorax; albuminuria, added tricuspid insufficiency with decided hypotension and lowered pulse pressure and the engorgement of the abdominal viscera.

Marked dropsy with mitral stenosis is due to the associated insufficiency of the valve; with stenosis alone, it is not likely to be extensive.

The pulse, with good compensation is small, regular, of good force and of nearly normal frequency. The pulse is easily obliterated by pressure, but under favorable conditions it is palpable between the beats.

Blood pressure may not be changed. The greater difference is in the *reduced pulse pressure* because the arterial tree compensates in a large degree; the minimal pressure rises because of the vasoconstriction. The difference between systolic and diastolic pressure is not so marked as in well compensated mitral insufficiency.

The *process of cicatrization* may continue in the muscle, change the chordae tendinae, "impairing at other places the functional activity of the heart muscle, and affecting the a.-v. bundle, depressing conductivity or producing nodal rhythm, thereby profoundly modifying the nature of the rhythm of the heart" (Mackenzie).

With marked incompetence of the valve and stenosis, the character of the pulse is changed, it becomes rapid, small, partaking of the character of the "mitralized pulse."

Mitral stenosis which develops early in life is more serious than when developed in adult life, because of the tendency toward increase of obstruction and the further fact, that the stenosed opening does not increase in size while the growth of the heart is progressive. Moon says that "such cases seldom reach the age of forty." Broadbent gives the average age at death of these cases at thirty-three years for men, and thirty-seven years for women. Hirschfelder thirty-three and thirty-eight respectively.

The significance of mitral stenosis in women is considered in connection with marriage and valvular disease.

When the second sound is inaudible at the apex, there is great danger of decompensation, any added effort proves the presence of muscular insufficiency.

The progressive character of the lesion in many cases accounts for the change of physical signs and other symptoms.

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Fading or weakening of the presystolic murmur, with diminishing second pulmonary sound is evidence of failure of the right ventricle.

The presystolic murmur is likely to disappear with the appearance of continuous irregularity of the heart and rapid pulse.

Mitral stenosis associated with arteriosclerotic endocardial change offers a less favorable prognosis than do other forms of the disease. *With the arteriosclerotic form of the disease, arhythmias are more frequent and often denote myocardial degeneration.*

Aortic Stenosis (*obstruction*).—Probably the majority of murmurs heard over the aortic valve are not due to true organic stenoses. Pure aortic obstruction is exceedingly grave. The murmurs are either functional (hemic), of arteriosclerotic or inflammatory origin.

Romberg analyzed 670 cases of valvular disease and found 17 uncomplicated aortic stenoses—2.53 per cent. At Johns Hopkins Hospital aortic stenosis was found in 5 per cent of the valvular diseases.

In practice it is found that most aortic stenoses after middle life are of arteriosclerotic origin, and that an aortic systolic murmur is often the first sign of the presence of the process; under such conditions there is increase of the second aortic sound with or without raised blood pressure.

Hypertrophy of the left ventricle is a necessity to overcome the effects of aortic obstruction when it is decided.

Marked dilatation is evidence of added insufficiency of the valve, a frequent combination; in these cases the pulse gives additional evidence for prognosis.

The loud systolic murmur is often out of proportion to the amount of obstruction offered by the uneven or contracted cusps.

Dilatation in varying degree is produced by aortic stenosis; *hypertrophy of the left ventricle is more dependable and lasting with aortic stenosis than with any other valvular lesion.*

Unfavorable Cases.—The unfavorable cases are those in which the obstruction is progressive, in which there may also be invasion of the coronary arteries and with final aortic insufficiency, dilatation, secondary distant changes and arteriosclerotic changes in the kidney, with obstruction in the peripheral vessels. The terminal stage includes aortic insufficiency with myocardial degeneration and the usual picture of decompensation.

The graphic study of the pulse offers valuable prognostic data.

As a rule, in favorable cases the pulse is slow, regular, of good force, and the artery is easily palpable between beats. The pulse wave is small, is well sustained, its rise and fall are slow. The *pulsus tardus* is not unfavorable. The *pulse tracing is more characteristic than with most other valvular lesions.*

Arhythmia shows itself in irregularity, in serious cases—the pulsus

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alternans and in occasional periods of *extrasystoles*, these depend upon the condition of the myocardium. True *alternating pulse is always of serious significance.*

Blood pressure depends largely on the amount of sclerotic change in the peripheral vessels and in the aorta, as well as on the condition of the myocardium, the kidney vessels and many other factors. In the average case without serious complications the pressure is normal.

Sudden death is less frequent than with aortic insufficiency; in most cases, long periods of symptoms of myocardial insufficiency precede death. This is not true of cases complicated with coronary disease and advanced myocardial weakness.

Mitral stenosis is favorable to the development of pulmonary tuberculosis. (See Tuberculosis.) Babcock found seven of his twenty cases of aortic stenosis with pulmonary tuberculosis.

The prognosis of aortic stenosis will often be favorably influenced by the revelation of the Wassermann reaction of the blood and its prompt acceptance for therapeutic indications.

Aortic Insufficiency.—Since the original classification of the disease by Corrigan, two forms of insufficiency have been considered:

(a) The Functional Form.
(b) The Organic Form.

(a) *Functional Form.*—The functional form is due to the dilatation of the mouth of the aorta and is associated as a rule with aneurismal dilatations of the aorta or it is an accompaniment of pulmonary insufficiency. It is exceedingly difficult to diagnosticate functional aortic insufficiency; I do not remember to have met with a case in which the diagnosis seemed to have been justified save as I found the aortic mouth wide open post mortem in connection with disease of the aorta.

(b) *Organic Form.*—At this point we must once more impress upon the clinician the great value for prognosis of recognizing the character of the lesion, whether inflammatory (endocarditic) or arterial and degenerative (arteriosclerotic).

When *rupture of the valves* occurs from mechanical strain or traumatism, it is associated with either ulcerative or sclerotic change, therefore requires no separate consideration. This question has an important *medicolegal bearing.* I do not believe that rupture of the normal valve follows strain or accident. Experimentally it cannot be ruptured by the highest pressure to which it is ever subjected by man.

The larger number of aortic insufficiencies are found in men, are of the arteriosclerotic form, are most frequent after middle life and depend upon the same factors for their production as general arteriofibrosis. A large number are of *syphilitic origin;* this is especially true of the many cases which have no history of acute endocarditis preceding and

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develop between the third and fourth decade of life. *The positive Wassermann reaction proves the truth of these conclusions.*

The heart changes depend entirely upon the fact that the left ventricle is forced to supply the arterial tree with sufficient blood; this it can only do by compensating for the return of blood to its cavity during diastole through the insufficient valve which during systole was forced into the aorta.

Naturally the amount of extra work thrown upon the left ventricle and the seriousness of the lesion depend upon the size of the leak, the length of time of the regurgitation, the pressure which must be overcome in the arterial system (aorta particularly) and the extent of associated lesions in distant organs.

Aortic insufficiency offers an unfavorable prognosis because the larger number of cases are advanced before treatment is instituted and being dependent upon arteriosclerosis are likely to be progressive.

In the moderately advanced cases or where the processes are stationary patients may live during many years with compensation which makes light occupation possible and life comfortable.

The *endocarditic type* offers a much better prognosis than does the arteriosclerotic.

Arteriosclerotic insufficiency in young subjects with evidences of progression, uninfluenced by specific treatment advances rapidly to a fatal termination with a number of complications in distant organs.

The *Flint murmur, presystolic,* heard over the mitral area accompanies many cases of aortic insufficiency. Austin Flint first described this murmur and claimed that it was due to the functional narrowing of the orifice between the mitral cusps which was closed at the beginning of auricular systole. There has been much discussion and controversy over the true cause and significance of the Flint murmur. (Thayer, Guiteras, Gibson and others.) The consensus of opinion is in favor of Flint's original contention, but for prognosis it must not be forgotten that *true mitral stenosis may complicate the organic lesion.* I have not found that the presence of the Flint murmur influenced the course of aortic insufficiency unfavorably.

So long as the left ventricle is sufficiently compensated pulmonary stasis is prevented, but with its failure and its persistent dilatation, it develops and is not easily overcome.

Blood pressure in the inflammatory form of aortic insufficiency is not so high as in the arteriosclerotic cases. A normal pulse rate with a nearly normal systolic and diastolic pressure is found only in cases without marked sclerosis and with very limited insufficiency.

Fall of blood pressure is often unfavorable, whether produced by a weakened myocardium or by drugs.

Hypertension and high pulse pressure are characteristic of aortic

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insufficiency and offer valuable data for prognosis as well as diagnosis. In no other cardiovascular disease is there such enormous difference in the maximum and minimum pressure. Once established, the general features of the Corrigan or trip-hammer pulse persist until changed by myocardial fatigue.

The wave is large, the upstroke sudden, the pulse is collapsed during diastole. *The sphygmographic tracing may be safely relied upon for it is characteristic and promptly shows the break when it occurs, which is due to extreme dilatation and myocardial revolt.*

In favorable cases the pulse rate is slow and regular. *With a rapid pulse, ventricular extrasystoles, evidence of dilatation and myocardial weakness, and the bigeminal and irregular pulse the outlook is serious.*

The laboring heart, thickened and *visible throbbing arteries* are evidences which must be studied with the associated features for the correct interpretation of their prognostic significance, also the *capillary pulse.*

The *snappy second sound* is found in cases in which the peripheral resistance demands the "slamming of the door" as Lauder Brunton has so forcibly expressed the phenomenon.

Suddenly arising mitral insufficiency (muscular relative insufficiency) is due to extreme dilatation of the left ventricle and is unfavorable.

The association of coronary disease with aortic insufficiency offers only the most dismal forecast and yet life may be prolonged by rational living in many of these cases. (See Angina Pectoris.) It is in these cases that family history is of great prognostic value.

The recurring strain to which the arteries are subjected by the enormous hypertrophy of the left ventricle in many cases is a factor in producing or increasing arteriosclerotic change.

The influence of arteriosclerotic changes in the brain, kidney, and within the splanchnic area is paramount. (See Cerebral Apoplexy, Arteriosclerotic Nephritis and Arteriosclerosis.)

Sudden death is more frequent with aortic insufficiency than with any other valvular lesion. (See same chapter, General Considerations.)

Subjective symptoms which are unfavorable include faintness, precordial pains, dyspnea, somnolence and mental torpor.

In the prognosis of aortic insufficiency no single symptom can serve to give a reliable forecast. The multitude of lesions which may be produced by the sclerosis, of which the valvular defect is only a part, takes the clinician into an enormous field. In the final analysis there are naturally many factors to be considered, but the paramount issue must always include the accommodation of the ventricle to withstand the strain by sufficient dilatation and hypertrophy, i. e., to hold compensation. "The field of cardiac response is the only true and safe guide" (Mackenzie).

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Tricuspid Insufficiency.—*Lesions of the tricuspid valve are rare.* In the preceding pages we have considered the association of tricuspid insufficiency with other heart and lung lesions. It is not likely to exist independently. It is frequently present as an expression of *muscular and relative insufficiency*, and with diseases of the lung or the left heart, it is always a serious complication.

The *recognition of insufficiency* is made possible by the accompanying *venous pulse* and *pulsating liver.*

True tricuspid insufficiency leads to death. We have no exception to report. Colbeck says "the precise estimate of the leakage is of less importance than the determination of the exact causes which have led to the occurrence of the lesion." The chief points to be considered are:

1. "The degree of enlargement of the right ventricle and auricle.
2. "The presence or absence of venous pulsation in the neck.
3. "The presence or absence of pulsation of the liver and the degree of enlargement of the organ.
4. "The degree of arterial anemia."

Tricuspid Stenosis.—Tricuspid stenosis is not found without insufficiency, compensation is out of the question (Romberg). Sphygmographic tracings may lead to the suspicion of the existence of the lesion.

Congenital defects are sometimes associated with fetal endocarditis causing tricuspid stenosis. (See Congenital Defects of the Heart.)

The *acquired form* is more frequent in women than in men and is secondary to mitral stenosis. The two lesions are almost always associated, and both are more common in women. The rise in pressure in the right ventricle following mitral stenosis "causes strain and irritation," and invites tricuspid change.

The right side of the heart is more frequently the seat of valvular murmurs with the malignant than with the usual forms of endocarditis.

The blood stream through the tricuspid orifice is obstructed and increased, demand is made on the right auricle, hypertrophy results with more or less dilatation. *The amount of dilatation also depends on the associated insufficiency of the valve.*

Unfavorable conditions with all tricuspid disease are congestion of the portal and general venous system. The amount of hypertrophy and dilatation of the right ventricle depends largely on the degree of mitral stenosis, as does the pulmonary engorgement also.

Defects of the Pulmonary Valve.—Most murmurs heard in the pulmonary area are of *functional hemic origin,* they are systolic and, considered alone, are of but little significance. *Cardiorespiratory murmurs and mitral murmurs* are often heard in the pulmonary area.

Stenosis is usually of congenital origin and predisposes to tubercu-

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losis. For a full consideration of its prognosis see Congenital Stenosis of the Pulmonary Valve.

Pulmonary Insufficiency.—*Pulmonary insufficiency is rarely acquired, it may occasionally be of syphilitic origin.* It occurs with *kyphosis, mitral stenosis and narrowing of the pulmonary artery or its branches,* when it is a relative insufficiency. *Aneurism of the aorta* may also be associated with relative pulmonary insufficiency (Romberg).

Barie reports 58 cases and claims that it may be an *acquired lesion* most frequent between the ages of eighteen and thirty-four. The *right ventricle* enlarges, there is great *venous congestion, jugular and hepatic pulsation, cyanosis and clubbed fingers.* The *prognosis* is only favorable so long as the right ventricle proves sufficient. The regurgitation is probably slight if the murmur does not efface the second sound.

The complete effacement of the second sound is evidence of serious insufficiency of the valve.

3. *Arteriosclerotic and Syphilitic Endocarditis*

The influence of the degenerative types of valvular disease depending on *arteriosclerosis* and *syphilis* is fully considered in this chapter and in connection with the study of *cardiovascular syphilis* and need not be repeated. *The progressive and unfavorable cases of valvular disease are those of the degenerative or arteriosclerotic type, particularly between the twentieth and fiftieth year. In older individuals the process is better borne and may remain stationary during many years.*

The beginner may be led by the presence of a systolic aortic murmur with moderate arteriosclerosis to offer a grave prognosis, this is not justified in the average case which remains under reasonable control.

The *blood pressure study* of these cases gives valuable information in connection with a thorough appreciation of the coronary circulation and the kidney function.

In the degenerative types of disease particularly, the frequent *Röntgen examination* and the use of *graphic methods* are a necessity for the valuable information which they add.

4. *Combined Valvular Lesions*

From the foregoing consideration of the acute and chronic cardiopathies it is clearly evident that combined lesions are more frequent than are the single defects.

We have seen mitral and aortic lesions together with full compensation during many years and death resulting from intercurrent disease.

The mitral lesions combined, as has been shown, may also continue

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without causing serious inconvenience in many cases; there are always the dangers of decompensation to which we have repeatedly alluded.

There are combinations of lesions which act favorably; thus aortic stenosis may reduce the amount of regurgitation in aortic insufficiency, and the same occasionally happens when stenosis and insufficiency are combined at the mitral opening. The prognosis of the lesions included in the combination can only be given after the consideration of the facts mentioned in connection with the individual valvular defects.

Romberg's statistics show mitral insufficiency and mitral stenosis combined in 19.7 per cent alone, and in 7.97 per cent with valvular lesions. Aortic and mitral insufficiencies were combined in 12.69 per cent. In 4.93 per cent aortic and mitral insufficiencies with mitral stenosis were combined. The gravest combination is aortic insufficiency and stenosis 5.2 per cent. In 4.05 per cent there were besides aortic insufficiency and stenosis other valvular lesions. Tricuspid and mitral lesions were combined in 1.97 per cent of Romberg's cases.

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G. Functional Disorders of the Heart

In most cases the functional disorders of the heart are not diseases per se, but include the symptoms which are produced by the derangement of the nervous or muscular mechanism of the heart, or both; associated with true organic lesions. There are exceptions to this definition but as Colbeck has truly said, after committing himself to practically the same definition, "In other words, 'functional disorders' of the heart form part of many different groups of symptoms, which severally constitute 'a disease' properly so called. A clear grasp of this conception will go far to dissipate much of the difficulty and confusion that has grown up around the subject of functional affections of the heart."

Functional affections of the heart which include among their leading symptoms, palpitation, arrhythmia pain and a train of neurasthenic symptoms, may arise from changes in many organs. We find functional disturbances with all cardiovascular diseases, affections of the nerves and ganglia of the heart, the pericardium, the myocardium, the aorta and

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coronaries, with arteriosclerosis and with vasomotor disturbances which influence arterial pressure.

Diseases of the nervous system are often associated with functional disturbances of the heart. *Neurasthenia* and *hysteria* are prominent among these.

Grave organic diseases of the brain and cord—tabes dorsalis, meningitis, brain tumor, apoplexy, epilepsy, injury to the brain, lesions of the medulla, mania, manic depressive states and general progressive paralysis, all, at some time during their progress develop characteristic evidences of functional derangement of the heart.

The *thyroid heart* (hyperthyroidea) is separately considered. (Diseases of the Ductless Glands.)

The influence of the diseases of the lung, tuberculosis particularly, is paramount in causing disturbed heart function and is separately considered. (Tuberculosis.)

The large number of *neurasthenics* with *derangements of the gastro-intestinal tract* adds an enormous material in which nervous manifestations are in the foreground. *These cases include neuropathics with ptoses (Glenard's Disease) who are rarely without phobias of some kind, due to deranged function of the heart of reflex character.*

The influence of *constitutional diseases* including all forms of *anemia, gout, diabetes, so-called rheumatism, the leukemias,* the *acute and chronic infections,* each is a factor in producing perverted heart function.

In considering myocardial disease and hypertrophy we mentioned the *influence of masturbation, ovarian and uterine disease.*

Toxic states, including uremia, acidosis, the excessive use of alcohol, tea, coffee, tobacco, each modifies the action of the heart. The effect of lead and other drugs including digitalis, strophanthus, aconite, belladonna, the bromids, and iodids, is largely influenced by existing resistance and idiosyncrasy when used in small doses, when in larger dosage, the physiologic effect on the separate functions of the heart are promptly manifested. We consider among the functional derangements:

1. Palpitation.
2. (a) Paroxysmal Tachycardia and (b) Simple Tachycardia.
3. Bradycardia.
4. Arhythmia.
5. The Neurasthenic State.

1. Palpitation

The sensation which is distinctly perceptible to the individual, caused by the undue frequency of the regular or irregular heart, is known as *palpitation.* It is probably the most frequent of all sensations referred

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to the heart, *causes in the overwrought and neurasthenic or nervous patient the fear of death and in the majority of cases is not associated with organic disease of the heart.* Palpitation in most cases is due to influences which act through the nervous system and is caused by hurry, worry, excitement, fatigue and kindred factors which are evanescent in their effect. The subjects whose hearts are promptly ungeared belong to the neurasthenic class—true neuropaths.

Palpitation may be an expression of a weak heart muscle, when, as a rule, there are extrasystoles. Hirschfelder has demonstrated that palpitation may persist "without any motor disturbance in the heart's action and without any change in the reflex response of the heart to various stimuli."

The majority of palpitations are without serious significance and exist without organic disease of the heart.

In the majority of cases in which the symptom is not of organic origin it either disappears suddenly to return when depressing or toxic factors are added, or it yields after a painstaking investigation of the patient's history leads to the relief of its cause. In all cases which remain unexplained by physical examination the possibility of tea, coffee, tobacco, alcohol, coal tar preparations, thyroid extract and other drugs as the possible exciting cause should be considered. *Distant and unexpected lesions are often recognized as provocative of palpitation, their relief is followed by the disappearance of the rapid heart.*

The *disagreeable and depressing mental pang* which neurotics suffer with palpitation makes them wretched during the continuance of the symptom.

The palpitations due to the infections, usually during the period of convalescence (pneumonia and diphtheria particularly), offer a good prognosis with rest and reassurance.

Palpitation with menstrual anomalies at the *menopause, puberty* and *during menstruation* may appear serious at times, but always yield when without organic fundament.

There are some women, men occasionally, who from the slightest imaginable cause between the fifteenth and about the thirty-fifth year of life promptly "blush and palpitate," in whom the attacks are evanescent, exceedingly annoying, but without effect on their general condition.

2. (a) Paroxysmal Tachycardia

For over half a century paroxysmal tachycardia has been recognized by the profession as a symptom complex without a clear conception of its nature or the method of its production. In all cases the striking features are those which were included in Bouveret's article and the works of A. Hoffman.

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Clinical experiences prove that in most cases the tachycardia begins without warning and ends with equal suddenness. Hoffman's tracings show the characteristic change of the heart rate within a single cycle. *The heart rate during the paroxysm is either double, treble, or quadruple that of the patient's heart rate just before the attack commenced.* These characteristics differentiate paroxysmal and simple tachycardia or excessive palpitation.

For our purposes of prognosis the differential diagnosis of the varieties of tachycardia is important.

My experience with paroxysmal tachycardia does not agree with those who claim that it is as frequent in men as in women. *I have rarely found paroxysmal tachycardia in men without positive evidences of hyperthyroidea, this is not true of women who have presented the uncomplicated idiopathic variety of the disease, which justified the diagnosis of paroxysmal tachycardia.*

The author does not consider those of auricular fibrillation with mitral stenosis (not infrequent) as essential tachycardia.

With serious attacks, pulmonary congestion may become alarming, the pressure in the pulmonary circuit is then high, while the systolic blood pressure and pulse pressure is usually low. *The alarming symptoms include the enormous tachycardia, pulmonary stasis, cerebral anemia, low blood pressure and pulse pressure, occasionally dyspnea and albuminuria.*

There are cases in which no remedy influences the paroxysm which yields without known cause and often leaves the patient without marked weakness.

In occasional cases sudden acute dilatation causes death after the tachycardia ceases. A case which we watched over twenty years, with attacks recurring at intervals of from three or four months to as many years, recovered from a slight attack, seemed uninfluenced; the following day while shopping she fell forward on the counter and immediately expired. This is not a frequent occurrence.

The fluoroscope has demonstrated to the satisfaction of those who have had opportunity to examine the heart during the attack, that the heart is not dilated but is decreased in size and that in severe cases it dilates toward the end of the paroxysm.

The embryonic sounds (originally so characterized by Nothnagel) are heard during the attack.

In the more severe cases the liver remains permanently enlarged.

The duration of paroxysmal tachycardia is variable. I have had two cases under observation (both women) during the past twenty years. Occasionally the seizures cease after a few years of recurrence. The only death in our series is above mentioned after insufficient rest following an apparently insignificant paroxysm.

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Osler reports a case of H. C. Wood in a physician "who in his eighty-seventh year had had attacks at intervals from his thirty-seventh year." In this case "the taking of ice-water or strong coffee would arrest the attacks." When the attacks cease all patients promptly recognize the "flop" for which they have learned to wait.

2. (b) Simple Tachycardia

An abnormally rapid heart in which the individual is as a rule unconscious of the beat, which is without the features of paroxysmal tachycardia, may be considered simple tachycardia. In many cases tachycardia is physiological, as during pregnancy, during lactation; there are perfectly normal hearts which continue abnormally rapid throughout life without causing inconvenience.

The *abnormally rapid hearts and their baneful influence on prognosis of the acute infections are considered with the separate diseases.*

In all acute infections prolonged tachycardia is evidence of serious cardiac toxemia.

It must be accented that *tachycardia during the incipient stage of most acute infections is evidence of virulent infection and vasomotor paralysis.*

Tachycardia with cerebral lesions is evidence of a lesion of the pneumogastric nerve, which is due to an anatomical lesion of the nerve or to pressure which after a period of irritation led to paralysis.

Causes.—Thrombosis and embolism, brain tumor, bulbar paralysis, myasthenia gravis, Landry's paralysis, acute myelitis, acute poliencephalitis, lateral sclerosis (amyotrophic), disseminated sclerosis and hemorrhage of the fourth ventricle are mentioned by von Neusser among the causes of simple tachycardia. Charcot and Oppenheim also mention the crises of tabes and syringomyelia with bulbar manifestations.

There is no disease of the brain or cerebral injury (fracture included), which may not cause tachycardia. In all cases tachycardia influences prognosis unfavorably but the prognosis depends entirely on the nature and extent of its cause.

Irritable hearts and delirious hearts (*Delirium Cordis*) are associated with enormous rapidity of action, usually there is some precordial pain, the subjects are nervous individuals, easily ungeared. J. M. DaCosta reported the cases of 200 soldiers with fever and overstrain in 17 per cent, diarrhea with mild typhoid fever in 30.5 per cent; hard field service; excessive marching 38.5 per cent; doubtful causes in 18 per cent; in which there were irritable hearts.

Many cases of irritable hearts are associated with myocardial degeneration and demand a guarded prognosis. In some cases the irritable heart is found in young recruits unaccustomed to "the strain, mental

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excitement and insufficient training." Hypertrophy is occasionally followed by dilatation in grave cases.

3. Bradycardia

An abnormally slow heart is synonymous with bradycardia.

True bradycardia includes only those cases in which all of the heart chambers beat equally slow. The other forms of bradycardia according to Mackenzie are "false"—they are due (*a*) to a missed beat, in which the ventricle contracts, but the pulse wave because of the feeble contraction fails to reach the wrist, (*b*) "certain cases of nodal rhythm where the auricle has ceased to beat, or does so synchronously with the ventricle," and (*c*) "where the stimulus is blocked between auricle and ventricle so that the auricle beats at its normal rhythm and the ventricle does not respond to the auricular systole, but pursues an independent and slow rhythm" (heart block).

Bradycardia is not necessarily pathologic. There are individuals who always have a slow pulse and are never influenced unfavorably thereby.

During labor, the pulse may be normally slow.

The leading causes of bradycardia summarized by von Neusser are:

Toxic substances:
- Tobacco—Nicotine
- Lead
- Physostigmin—Muscarin
- Potash salts—Picric Acid.

Autotoxic substances:
- Ptomain poisoning
- Bile
- Urea
- Acetone—Acetic Acid.

Convalescence from Acute Infectious Diseases—Rheumatism and *Pneumonia* particularly.

Stokes-Adams Disease.

Coronary and Myocardial Disease.

Diseases of the brain:
- *Gummata, Tuberculous and other tumors*
- *Lesions of the medulla oblongata*
- *Hyperemia of the vagus center*
- *Meningitis*
- *Concussion of the brain*
- *Cerebral apoplexy*
- *Thrombosis and Embolism*
- *Acute hydrocephalus*

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Hemorrhage of the fourth ventricle
Facial Paralysis
Cysticerci of the fourth ventricle.
Hysteria.
Melancholia.
Basedow's Disease (during transition from Basedow to myxedema).
Pressure on the vagus:
Carcinomatous glands and tuberculous growth of the neck.
Cancer of the Stomach, gastric ulcer and gall-stone colic.
Injuries to the spinal cord.
Diseases of the Ear:
Foreign bodies in the external ear; reflex irritation from the auricular branch of the vagus.

Each of these many possible causes of bradycardia suggests its own prognosis.

When bradycardia arises suddenly during the active period of pneumonia or any grave infection, it usually indicates incipient meningeal invasion. During the period of convalescence it is not usually of significance with proper care and is not infrequent.

With *cerebral hemorrhage* moderate bradycardia is more favorable than tachycardia, which with high temperature is almost always fatal.

With *cancer of the stomach* bradycardia during the early stage may assist in diagnosis, for it is not infrequent and may, by leading to prompt recognition influence prognosis favorably.

Bradycardia due to syphilitic lesions offers a favorable prognosis—when attacked early and vigorously.

Heart block has been separately considered. The *influence of digitalis* and kindred remedies in slowing the heart must be considered in connection with the study of individual cases.

4. Arhythmia

The Arhythmias have been considered in connection with the diseases of the myocardium.

5. The Neurasthenic State

There are but few neurasthenics without complaints referable to the heart. These complaints are numerous, vary from day to day and are always interpreted as serious by the patient who soon becomes self-centered with the heart symptoms in the ascendency.

There are often acute exacerbations of symptoms resembling organic

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crises which are aggravated by the autosuggestion and associated fear of the patient.

In some cases symptoms continue during long periods; in other cases nocturnal attacks and periodicity are characteristic.

Anginoid attacks with marked development of an emotional element accent the fears of the neurasthenic.

Some patients are fairly well between the acute attacks but live in fear of this recurrence.

The mental pang suffered by the cardiac neurasthenic is often pitiful.

The pulse shows great variations in frequency and in character at different times, and under varying conditions. It may be surprisingly slow at one time, exceedingly rapid at another. *Intermission and arhythmia* with marked excitement and great fear of impending danger and associated hysteria are noted in some cases.

Sensory symptoms referable to the extremities, with hyperesthetic areas, at times to the precordium are frequent, and add to the discomforts and fears.

The prognosis of the neurasthenic state is favorable. The most potent factor in its prognosis is the personal equation of the attendant whose tact and resources will often be taxed during long periods, but by so regulating the lives of these individuals as to remove them from themselves and substituting a healthy suggestion for the ever recurring and depressing autosuggestion and other appropriate mental pabulum, these patients make satisfactory recoveries.

Relapse is frequent when depressing factors are usually responsible.

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Section IV

Diseases of the Blood and Hemopoietic Organs

A. Anemia

1. Symptomatic Secondary Anemia

Formerly the term "Anemia" included only a reduction in the number of red blood corpuscles. Anemia is now defined as a condition in which the blood as a whole, the red blood corpuscles or the hemoglobin, or both, are diminished.

Oligemia includes a condition of the blood in which all of its constituents are diminished.

Oligocythemia is a condition in which the red blood corpuscles are reduced.

Chlorosis or *oligochromemia* denotes a marked reduction in the amount of hemoglobin in the individual cell.

Local anemia or ischemia is usually either transitory or permanent. I consider both these conditions in connection with *vascular spasm* and *arterial changes,* such as endarteritis, which may choke the parts beyond the point of obliteration and lead to deep tissue changes—gangrene, necrobiosis and cyanosis (See separate diseases).

General Anemia

The larger number of anemias are of secondary origin and symptomatic.

Anemia due to loss of blood may be (a) acute or (b) chronic.

(a) **Acute Anemia (Hemorrhagic).**—Hemorrhage may cause sudden acute anemia reducing at once every element which normally floats through the vessels and naturally the amount of blood.

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Suddenly arising pallor, anemia, should always lead to the suspicion of hemorrhage. When external, the recognition of the cause is easy; when hemorrhage is internal, it is more difficult. With typhoid fever, sudden pallor and collapse without symptoms of peritonitis or intestinal perforation should always lead to the suspicion of intestinal hemorrhage, the blood may be held in the intestine for several hours before it appears in the stool. (See Typhoid Fever.) *Sudden anemia in women whose menstrual flow has been irregular or absent,* should always lead to the strong suspicion of *ectopic pregnancy with tubal rupture.* The prognosis of this condition is brilliant in cases recognized early and promptly treated radically. The clinician will make no more satisfactory conquests in the practice of his profession than in the prompt diagnosis of ruptured tubal pregnancy. These patients may be thoroughly exsanguinated and still recover. Accidents during delivery, placenta previa, uterine inertia, and laceration may cause serious and threatening depletion.

Malignant growths ulcerating or rupturing, may cause sudden and fatal anemia. One of our cases died suddenly from internal hemorrhage due to the rupture of a rapidly growing encephaloid cancer of the liver.

The ability of the individual to immediately furnish much of the water content of the separate organs to the blood vessels as these are depleted by sudden hemorrhage, is one of the important factors in saving life in acute anemia resulting from hemorrhage, by tiding him over the critical period.

Patients who are depleted or below par, do not bear sudden loss of blood well, for the response to the added demand on the bone marrow is slow and unsatisfactory. *The young and healthy bear the loss of blood better and react quicker than do older subjects.* It has been found experimentally, that with the loss of from $\frac{1}{4}$ to $\frac{1}{3}$ of the total blood volume (1/13 of the body weight) regeneration usually follows in from 2 to 6 weeks (Türk). Bierfreund found that with the loss of 25 per cent of the entire blood in children, complete regeneration followed in $22\frac{1}{2}$ days, in healthy adults in $17\frac{1}{2}$ days, and in the aged in 28 days.

It may be assumed that *oligocythemia* and *oligochromemia* are conditions which, with the *reduction of the blood plasma* are promptly compensated by nature's processes. The danger point in all acute hemorrhage is reached if one-half or more of the entire volume of blood is lost. Morawitz says that "the loss of more than two liters must be viewed with great concern and offers an unfavorable prognosis." A low blood count and cellular changes which show lack of regenerative power and marked enfeeblement is an unfavorable combination. If the underlying factor is removable, even under these threatening conditions, recovery often follows. Türk makes the unqualified statement that the exhaustion of the patient offers the indications for the immediate attempt to

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overcome the prime factor because extreme conditions may ultimately yield to radical treatment.

The plasma of the blood increases first after depleting hemorrhage, the regeneration of the red blood corpuscles is slower, while the hemoglobin is last to return to the normal level. Sudden hemorrhage stimulates both the erythroblastic and myelogenic tissues to activity, which accounts for the prompt *leukocytosis* (*posthemorrhagic leukocytosis*) which follows the loss of blood. The return of *normoblasts* and young red cells in abnormally large numbers is always favorable. The leukocytosis and excess of normoblasts, if present, are promptly changed to approximately average conditions.

The pulse may be small and rapid, the heart sounds distant and feeble, the associated symptoms extreme; all these conditions usually yield with the control of the hemorrhage. The prognosis must depend finally upon the cause of the hemorrhage, the extent of damage done to the tissues, the resistance of the patient and a variety of other conditions which present in the individual case.

(b) **Chronic Anemia (Hemorrhagic).**—The anemia which is chronic and associated with hookworm disease, has been separately considered (See Ankylostomiasis). Long continued drain leads to chronic blood changes. The gravity of the anemia depends upon the amount and duration of the hemorrhages, its localization and the cause. The leading causes of chronic hemorrhagic anemia are excessive menorrhagia, metrorrhagia, bleeding piles, intestinal and gastric hemorrhage due to ulcers of the duodenum, intestine or neoplasms (cancer), varices, epistaxis, purpura, hemophilia, hematuria due to organic disease or parasites.

The grave anemia of *bothriocephalus latus* is separately considered (See Pernicious Anemia and Bothriocephalus Anemia).

The *blood changes of chronic* (*hemorrhagic*) *anemia* include a characteristic picture. In extreme cases hemoglobin may sink below 20 per cent, and if the cause can be overcome, complete return to health usually follows. *In the grave types* normoblasts, polychromatic erythrocytes, megaloblasts and megalocytes are found. *In the more favorable cases* normoblasts, polychromatic erythrocytes, poikilocytes and microcytes are present. The *red count* falling below 1,000,000 in the acute and chronic cases is always ominous with the correspondingly low color index. Türk says 20 per cent of such cases offer a doubtful prognosis.

The *secondary chronic anemias* due to *malignancy, cachexia* and *infection* influence the forecast of these conditions.

Tuberculosis, cancer, sarcoma, nephritis, typhoid fever, malaria, the intoxicants, including lead, mercury, arsenic, antimony and other poisons are all associated with more or less anemia as these diseases advance. There is slow "latent bleeding" due to malignant growths of the intestine which during long periods offers no subjective or objective symptoms

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save gradually increasing anemia, the cause of which may be detected by the presence of *occult blood in the stools.* The prognosis of all depends upon the ability to remove the cause. The slow bleeding of cancer (gastric and intestinal) is likely to show greater cachexia than anemia and this is of value in differentiating pernicious anemia, in which the anemia is out of proportion to the cachexia. Faulty living, ventilation, diet and social conditions influence the blood state besides leading to primary conditions upon which anemia is usually dependent. With chronic bleeding and associated anemia or any form of secondary chronic anemia the unfavorable features include besides heart weakness and the unfavorable blood picture, edema, vertigo, tinnitus aurium, headache and dyspnea.

In *cases which are operable* the prognosis is best in which the hemoglobin per cent does not fall below 40. Von Noorden believes that any form of anemia may ultimately lead to complete exhaustion of the bone marrow which may present the clinical features and the blood picture of pernicious anemia. If this is true the occurrence is exceedingly rare. The author has never in practice seen a case of secondary anemia develop the pernicious or essential disease.

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2. Primary or Essential Anemia

(*a*) *Chlorosis*

(*Green sickness, Oligochromemia*)

Chlorosis is a condition of the blood in which there is a decided lowering of blood coloring matter—hemoglobin—which is limited to the female, is likely to develop during the period of sexual development, is relieved by iron, is never *per se* a serious disease, though it recurs easily, is materially and promptly influenced by the general condition of the patient. The *blood picture* of chlorosis is characteristic. Chlorosis may be diagnosticated in the absence of the picture of true anemia when there is a decided reduction in the percentage of hemoglobin. Most chlorotics

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are also oligocythemic (red corpuscles reduced). In the severe cases the red corpuscles number from 2,500,000 to 3,500,000 per c. mm. Hayem reports extreme counts as low as 1,300,000 per c. mm. Cabot averaged 77 cases at 4,050,000 per c. mm. Bramwell averaged 89 cases at 3,437,000 per c. mm. Mild cases show but slight reduction in the red count. Besides the reduced hemoglobin, there is an excess of blood serum (polyplasma), the regenerative power of the blood is reduced, the leukocytic count is not materially disturbed, the blood platelets are increased. The pathologic cause of chlorosis is unknown. Virchow believed that there was, in most cases, a congenital narrowing of the larger blood vessels (aorta).

Extreme chlorosis is associated with marked subjective symptoms; prominent among these are dyspnea, palpitation, exhaustion, menstrual anomalies, gastro-intestinal disturbance, obstipation and excessively developed emotional element, perverted appetite, vertigo, tinnitus aurium and the characteristic pallor of the mucous membranes and green colored skin. The extremities are cold much of the time. Chlorotics lack normal resistance. In these cases *hemic murmurs* (systolic) are usually present. The foregoing features are present and persist until relieved by some form of treatment. The majority of chlorotic girls yield to proper diet, ventilation and prolonged rest. *Uncomplicated chlorosis always yields to iron and other rational treatment.* No patient dies of chlorosis unless there has been some complication. *Pulmonary embolism and thrombosis* are rare but fatal complications; many men of large experience have never met such cases. The tibial or femoral vessels are occasionally the seat of thrombosis. With improvement of the general condition the color index is raised, the blood picture changes and all attending symptoms gradually yield. The return to a normal condition is often exceedingly slow and an irritable heart may persist during varying periods. The perverted appetite is also a source of annoyance in some cases during long periods. *Chlorotics are liable to relapse on slight, sometimes without known cause;* seasonal and climatic influences are powerful. Change of scene with rest often effects lasting cure.

Progressive loss of weight with chlorosis or any form of anemia argues against uncomplicated blood changes and demands search for the underlying cause before a forecast is justified.

The influence of intestinal toxemia in continuing or causing chlorosis should be considered in the individual case. Sir Andrew Clark strongly advocated the intestinal origin of chlorosis and believed that constipation was the leading factor.

In America, foreign girls between the ages of 12 and 16, shortly after their arrival, often become chlorotic and amenorrheic. This condition usually yields after a few months of treatment. Girls coming to cities from the country also develop chlorosis very frequently and menstrual

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anomalies. It has been noted that recurrence is finally prevented by pregnancy. Occasional cases remain but slightly changed during long periods; they are veritable *chronic chlorotics* without many annoying symptoms, but the blood picture does not return to normal. Some of these continue chloranemic throughout their lives. Among the frequent complications of chlorosis is gastric ulcer. The prognosis of this condition is separately considered. (See Gastric Ulcer.) Chlorosis with exophthalmic goiter is repeatedly met in practice and usually yields with the other symptoms of hyperthyroidea. Acute nephritis and endocarditis mentioned by Bramwell as sequelae of chlorosis we have never experienced. There is a strong tendency to self cure after the twenty-fifth or thirtieth year.

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(*b*) *Pernicious Anemia*

(*Addison's Anemia* (1855), *Progressive Pernicious Anemia, Malignant Anemia, Infectious Anemia, Biermer's Essential Anemia, Megaloblastic Anemia*)

Pernicious anemia is a chronic progessive, possibily infectious disease characterized by (*hemolysis*) *destruction of large numbers of red blood corpuscles* in which the remnant of corpuscles contains a *high hemoglobin* per cent; the disease presents a blood picture which is classic, though not absolutely pathognomonic; it often shows long periods of latency, has periods of exacerbation which are followed by remission in some cases, may either early or late present striking features showing involvement of the nervous system and in almost all cases leads to death with symptoms of toxemia. In rare cases the course is *acute*. There are besides the destruction of the blood elements, marked changes in the bone marrow, surprising retention of the body fat in spite of advancing disease, hemorrhages into the skin and serous cavities, dilatation of the heart, also myocardial degeneration, usually atrophy of the gastric and intestinal follicles; in the terminal stages, enlargement and fatty degeneration of the liver, which organ contains an excess of iron, with or without slight enlargement of the spleen. As a rule, the spleen remains negative so far as its size and contour are concerned. The changes in the bone marrow

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are easily recognized. The color is abnormally red, lymphoid cells and a large number of normoblasts (Ehrlich's gigantoblasts) are seen. Lichtheim first called attention to the symptoms and changes in the nervous system. These are important in the diagnosis and prognosis of individual cases and include sclerosis of the cord in patches, mainly affecting the posterior columns and the ganglionic cells of the sympathetic. I characterize the nervous symptoms as *"Lichtheim symptoms"* and will again refer to the complex. There is no treatise which details the clinical history of the disease more accurately than that given by Addison in 1855 under the caption of *idiopathic anemia.*

History.—Grawitz in considering the history of pernicious anemia mentions Combe as having reported a case in 1822, another by Marshall Hall in 1843 and Lebert in 1853 and 1868 call attention to parallel cases developed during pregnancy. Cazenave, in 1860 with Lebert, called attention to essential anemia without pregnancy. Combe in reporting the original case wrote "A marked instance of a very peculiar disease—If any train of symptoms may be allowed to constitute anemia a generic disease, the following may be considered a sample of it. in its most idiopathic form."

The disease is known on the continent of Europe as *Biermer's Progressive Anemia* or *Essential Anemia;* the original classic description of the disease by Addison which antedated Biermer's redescription by at least 17 years had been practically ignored even in England; in spite of the fact that the colleagues of Addison at Guy's Hospital were acquainted with his description but little attention was given to its diagnosis until their minds were refreshed by Biermer's treatise. The failure to recognize this form of anemia during those days is accented by the fact that Pye Smith in 1882 presented a complete bibliography and was unable to gather more than 102 cases from various sources.

Heredity.—Any grave anemia, pernicious particularly, in which there is a strong hereditary element is likely to be rapidly progressive and long periods of latency are not frequent. We have in our cases noted the frequency with which several members of the same family are afflicted. It is not unusual to find one or more brothers and sisters, or one parent and one or several children with essential anemia; all running the typical course to death. We have never met a case of pernicious anemia in a child below the age of 15 years. Osler reports one case in a boy ten years of age. The large majority of our cases were between 33 and 40 years of age. We do not include a single case in our old or new series in which pregnancy or prolonged lactation caused the disease. Pepper; Channing and Gusserow called attention to the influence of pregnancy on the production of essential anemia. Probably with modern hematologic methods of differentiation most of these cases would now prove to be secondary and dependent upon long continued drain.

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Blood Picture.—The blood picture of pernicious anemia is sufficiently characteristic to lead to its diagnosis in the majority of cases. There are occasional exceptions for thorough hematologists have been forced to concede that rare grave anemias, non-pernicious, do present pictures which so closely resemble the pernicious type that error is possible.

Ehrlich contends that the blood picture alone is so characteristic as to make diagnosis possible. The dictum to which the Ehrlich school adheres is that "Megaloblasts and Megalocytes show megaloblastic degeneration and this is the main cause of pernicious anemia."

Bothriocephalus anemia which in cases not too far advanced offers a fair prognosis, presents blood features which are so closely allied to the essential pernicious type of the disease as to make differentiation impossible and most authorities agree that the blood pictures are parallel (See Bothriocephalus Latus). Unquestionably advanced *bothriocephalus latus anemia* cannot from the blood picture be differentiated from true pernicious anemia and such patients die with all of the clinical manifestations of essential anemia. I have seen recovery from grave bothriocephalus anemia follow the expulsion of the worm which is usually dead or sick and by its presence caused toxemia.

The erythrocyte count is lowered in the advanced or most serious cases to 1,000,000 per c. mm. or below. The average in our cases early has been between 2,500,000 and 3,500,000. The blood is pale yellow, abnormally fluid, and clotting is slow and unsatisfactory. In some cases the prick is followed by oozing and the surrounding skin becomes ecchymotic (spurious hemophilia).

Blood counts in which the erythrocytes fall below 1,000,000 are rapidly fatal. Prognosticating from the blood picture we quote Cabot:

"1. Severe (rapidly fatal)
- (a) Extreme progressive anemia.
- (b) High color index.
- (c) Increase in size of red cells.
- (d) Denegerative changes.
- (e) Numerous megaloblasts.
- (f) Few or no normoblasts.
- (g) Lymphocytosis."

"2. Less severe (slower course)
- (a) Remissions.
- (b) Normal or low color index.
- (c) Normal sized cells.
- (d) No degenerative changes.
- (e) Few megaloblasts.
- (f) Numerous normoblasts.
- (g) Normal percentage of adult cells."

The size of the red cells is increased—*megaloblasts* and *megalocytes* are abundant. There is marked *macrocytosis*—the number of small sized red corpuscles is striking and these vary in size and shape (*anisocytosis*). *Misshapen red corpuscles* (poikilocytosis) are abundant. The high *color index* (*high hemoglobin value of the individual cell*) is one of the constant features and serves in doubtful cases to make diagnosis and prognosis positive. *Polychromasia* is the rule. *Normoblasts* or *nucleated*

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red blood corpuscles are usually, but not always present. During the early history of individual cases (not acute or rapidly fatal) normoblasts are present. Their presence indicates response of the bone marrow to the stimulation necessary to make new blood elements. The *complete absence of nucleated red corpuscles may be interpreted as indicating failure to respond and is always of bad prognostic significance.* The myelogenic reaction which brands an anemia as pernicious and consequently fatal is of great importance. Neusser says "We find the expression of reaction of the bone marrow, which is regenerative, in the appearance of nucleated red blood corpuscles (normoblasts) while the production of megaloblasts with degenerated small and badly tinged nuclei are the expression of degeneration." The leukocytic count in the average case may not be materially changed but as the disease advances there is a reversion of the entire blood to the embryonic state. The presence of myeloblasts in increased numbers (5 to 10 per cent) is not unusual and blood platelets may drop to 75,000-100,000.

In our consideration of the subject we assume that pernicious anemia because of its uncertain pathogenesis should include "any profound and (apparently) causeless anemia which is characterized by peculiar alterations in the blood—which tend to pursue a progressive and pernicious course." (Bramwell.)

Bramwell believes that the question whether the clinical condition termed pernicious anemia "may result from a variety of causes or whether it is a singular clinical entity, the causation of which is always one and the same, should be left an open one." We are safe in concluding that in the typical cases there is excessive and rapid blood destruction (hemolysis) and defective blood formation.

For our purposes of prognosis the consideration of the unsettled theories relating to the etiology of the disease is unnecessary. Indeed the profession is by no means agreed. There are data both clinical and experimental which strengthen the *infectious and toxic origin* of the disease, that *increased destruction of blood in the portal system* is due to the *absorption of toxins from the gastro-intestinal tract,* and that *oral sepsis* (Hunter, Wm.) is an important factor in causation.

In considering various pathologic data which influence prognosis the frequency of *achylia gastrica* (Einhorn 1892—Martius 1897) associated as it is with *atrophy of the gastric follicles,* a frequent, almost constant attendant deserves consideration (Grawitz, Fenwick, Quincke, Nothnagel, Jurgens, Friedenwald). While Friedenwald does not subscribe to Grawitz's contentions that with achylia gastrica resulting toxemia, the hemolytic action of toxins elaborated in the stomach and intestines cause pernicious anemia; he found in 70 per cent of his pernicious anemias the presence of atrophy of the gastric follicles (achylia gastrica) and in 20 per cent of the remnant marked reduction of hydrochloric acid. Friedenwald

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believes that the same toxic agent is at once the cause of the achylia gastrica and the pernicious anemia.

Lazarus expresses the same view, believing that both conditions are the result of an unknown poison.

Faber and Bloch believe that the changes in the gastro-intestinal tract are post mortem and that there is no direct proof of the existence of such lesion *intra vitam*. This contention has not received support. We know that during life in most cases there is absence of free hydrochloric acid and we have often in our cases found long periods of improvement or latency follow the administration of free HCl. in large doses after the method of Croftan.

Whatever we conclude concerning the relation of achylia gastrica and essential anemia the fact remains that life is shortened by the complete anorexia and gastro-intestinal disturbances associated with atrophy of the gastric and intestinal glands. We have seen the more rapidly fatal course in those cases in which after a period of intestinal symptoms, *diarrhea* usually, hemolysis has been rapid, the general condition has promptly failed, complete anorexia and stomach intolerence has been marked and without remission, but with increasing involvement of the sensorium death has followed. There are a number of cases in which during years preceding the development of essential anemia, *chronic diarrhea* has been a prominent feature. This remains uncontrolled in most cases and finally, there are added the complete blood picture and other clinical features of pernicious anemia. These patients are not likely to have periods of remission or latency, but the onward march to death is prompt, with symptoms of sepsis.

Pernicious anemics without prominent and persistent gastro-intestinal symptoms live longer and are more likely to have periods of remission and latency than do those with such complications.

Grawitz who bases his pathogenesis on the absence of free hydrochloric acid in the stomach contents reports repeated cures. Critics are agreed that none of the cured cases have been proved to be true pernicious anemia. Grawitz does not consider the blood picture of pernicious anemia diagnostic and has, according to Türk, included all forms in his list of the essential anemias. Lazarus, Cabot, Türk and Naegeli disagree with Grawitz and believe that cases of primary hemolytic anemia in which there is a characteristic blood picture and in which there are positive evidences of the failure of the bone marrow to react to normal stimuli, are fatal.

Pernicious Anemia and the Spleen as a Hemolytic Organ.—The successful issue in Banti's Disease in which there are evidences of anemia and hemolysis which have followed *splenectomy* with the results of experimental research, have led a number of clinicians to consider the influence of splenectomy on the prognosis of pernicious anemia. The literature of this subject is growing and while in a few individual cases thus treated

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patients have withstood the operation, no positive conclusions are justified at the present time. Eppinger reports two cases of pernicious anemia without death following the operation. He believes that the extirpated spleens of pernicious anemia, hemolytic jaundice, and experimental toluylendiamin are identical, all filled with erythrocytes. The urobilin in the stools of all splenectomized patients showed marked reduction and convalescence was without incident.

Eppinger's material besides the two cases of pernicious anemia included 2 of hemolytic jaundice, 3 of Banti's disease, 2 of hypertrophic cirrhosis and one of grave catarrhal icterus. There are isolated cases in medical literature in which there seemed to be improvement but we are not justified in reporting any cured. We would further refer the reader to the reports of George Klemperer and Hirschfeld, Banti and the experimental work done by both American and German pathologists in this field.

Acute Pernicious Anemia.—There are cases in which pernicious anemia runs a rapid course to a fatal termination; such behavior is exceptional. I have recently seen a case in which, after a short period of indefinite "Lichtheim symptoms" within two weeks there was such prompt hemolysis and utter loss of marrow reaction that the blood picture of the gravest megaloblastic anemia was complete. There are cases of *syphilitic anemia* which we have met in families with positive hereditary tendency to pernicious anemia, in which the blood picture of the disease is completed within a few weeks. Such a case I now have under observation in which one parent and one brother died of pernicious anemia; a sister suddenly developed the cord symptoms which are often present early in the grave types of the disease, the hemolysis was most destructive, the count fell to almost 1,000,000 within two weeks, the cell elements and high color index were characteristic of true essential and pernicious anemia. The intravenous injections of neosalvarsan promptly brought relief of both objective and subjective symptoms. Such cases, before a positive prognosis can be given, demand long periods of observation for it is not at all safe to conclude even in the acute cases with positive Wassermann reaction and the blood picture of genuine pernicious anemia that the treatment has not proved sufficient to awaken the bone marrow to renewed activity and that later there will not be a return of classic symptoms and the onward march of the disease. Certainly the syphilitic history and the satisfactory reaction following salvarsan in acute cases argue in favor of a good prognosis in cases of grave anemia which in the end, if the patient remains permanently cured, proved that they were not true megaloblastic anemia.

With acute pernicious anemia marked *glossitis, gastro-intestinal symptoms, rapid loss of strength, dyspnea* and *symptoms referable to the central nervous system,* (brain particularly) the chances of remission are small and death may be expected before the end of the eighth week.

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While the sudden, severe and persistent character of blood destruction —hemolysis—is the feature which is in the ascendency even in acute cases, the striking power of regeneration is a factor which is paramount and it does in a proportion of cases, which begin with acute symptoms and rapid blood destruction (in the more favorable cases), lead to marked improvement, long periods of remission and the restoration of sufficient strength to return the patient to his work. Such patients may remain immune from symptoms during varying periods in spite of the acute onset and enormous hemolysis, but in the end the symptoms return; there may be several remissions but the end follows a period of continuous symptoms just as in those cases which were chronic and progressive from the beginning.

Remissions and Periods of Latency.—Nature's attempt to stimulate the blood producing organs to renewed activity after hemolysis is strikingly successful in over 50 per cent of all cases. Indeed it is the exception to find an idiopathic anemia which leads to a fatal termination without one or more remissions of varying length.

Cabot reports 524 cases of which

296	had	one remission
118	"	two remissions
65	"	three remissions
21	"	four remissions
24	"	five remissions

In 6,300 cases of internal disease tabulated, I have seen 46 cases of pernicious anemia, in over 75 per cent of these, remissions led to such marked improvement as to materially change the blood picture and not infrequently the original diagnosis has been doubted. I number among my older cases one of a young girl in whom I made the diagnosis from the positive blood picture 10 years ago, who improved and married, indeed the blood apparently became normal until within the past six months, when she returned after a short period of severe Lichtheim symptoms with a blood count of 1,510,000 erythrocytes; 7,800 white corpuscles, color index 1 + and the disease is now rapidly progressive. This case had the longest period of remission of any case in my experience. It proves that it is not safe to offer rose colored prognosis in these cases. I have never met true pernicious anemia, it matters not how long the period of improvement or remission, which did not finally lapse. The length of life depends upon the natural powers of recovery of the blood producing organs which as Hunter has said, "are very striking and constant," as well as upon the complications.

I would warn against the assumption that any particular form of medical treatment is the paramount factor in stimulating the inherent power of the bone marrow to regenerative function after even long periods

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of inactivity. It would seem that when hemolysis has produced the characteristic degenerative changes the bone marrow attempts to come to the rescue and as already suggested succeeds during varying periods.

Bramwell reports that one of his patients remained well for 12 years and then relapsed and died almost fourteen years after the first attack.

Nervous Symptoms.—I have repeatedly referred to "Lichtheim symptoms" in considering prognosis. These include a variety of subjective complaints, the leading early symptoms are a "numbness and awkwardness of the hands" often the legs are paresthetic at the same time. These paresthesias and accompanying reactions are often "tabetic" in character and include unsteadiness of gait and loss of patella tendon reflex. In rare cases pupillary changes are present as well as sphincter disturbances. It is interesting to note that paresthesias and disturbances of locomotion at times antedate anemia. In another group of Lichtheim cases there may be but slight paresthesia of the hands early, no tabetic symptoms, in which the nervous complex increased with progression of the anemia. There are, in the most severe cases, in which remission is scarcely to be expected, early evidences of *cerebral toxemia*, from which the patient may only partially rally to finally fall into profound coma. Such behavior is unusual, characterizes the terminal stage, but whenever there are profound mental disturbances the prognosis for life is bad and death promptly follows. While the gravity of the anemia is not in direct proportion to the nervous symptoms in all cases, our experiences justify the conclusion that once established, Lichtheim symptoms are likely to persist and that marked tabetic and cerebral symptoms when present are found in the most advanced stages or in those cases least likely to have long periods of remission. When remission is decided in cases with few Lichtheim symptoms the slight numbness and other abnormal sensations are usually borne without complaint. In my 46 cases of pernicious anemia among 6,300 patients over 80 per cent developed Lichtheim symptoms either early or late—usually during the first 12 months of the disease.

Heart and Blood Vessels.—With the initial hemolysis the pulse is small, thready and rapid with a low blood pressure and a strong tendency to edema of the ankles. *When the edema becomes general the myocardium is enfeebled and there is hydremia* in most cases. *Small, feeble, rapid pulse, low blood count, dyspnea, edema and evidences of toxemia showing themselves in increasing mental and nervous disturbances, form a complex which with the blood picture is characteristic of the terminal stage of the disease. Small feeble pulse with tinnitus aurium, vertigo* and *palpitation with some Lichtheim symptoms* and *low red count may still be followed by remissions, one or more. Edema of the lung* with feeble heart and other complications, marked enlargement of the liver and albuminuria are unfavorable, and soon lead to death.

Persistent tricuspid regurgitation, epistaxis and purpura are unfavor-

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able. Usually there is marked *edema,* at times *hydrothorax* and *retinal hemorrhage. Venous hum* over the neck veins (external jugular) may be present early and persists during the periods of exacerbation until the end; the same is true also of *hemic murmurs* heard best at the base of the heart. With an improved blood these murmurs may disappear.

Retinal hemorrhages may be an early or late complication. Probably 50 per cent of essential anemias have retinal hemorrhage at some time. The hemorrhages are not, as a rule, large. I have never seen a case in which the hemorrhage led to blindness. *Retinal hemorrhage and pallor of the fundus are of diagnostic and prognostic value. Deep purpuric conditions* once present, there is small hope of remission or improvement of the blood state.

Temperature.—Slight elevation of temperature is frequent. Some cases have a continuous slight elevation of temperature which does not seem to interfere materially with the disease. In most cases the higher continuous fever which is associated with other toxic symptoms—central nervous manifestations—is present late in the disease and is not influenced by treatment. The fever is almost always irregular and atypical. It is an expression of toxemia.

In chronic cases death is often hastened by acute exacerbations during which elevation of temperature is the earliest symptom. Such cases may be following a typical course, with periods of remissions, when without known cause, there may or may not be a chill; continued fever, not always high, but with a slight morning fall persists. With increasing malaise and extreme exhaustion and increasingly rapid and small pulse, symptoms of toxemia including delirium and coma follow. The temperature curve is between 100½° F. and 103° F. (may be higher). Death may be expected before the end of the fourth week. The mental (toxic) symptoms are always prominent from the beginning of such exacerbations.

The *urine* offers no marked features to influence prognosis. Cases which show no tendency to improve may often die without showing a trace of albumin. In other cases as already suggested, with general dropsy in the terminal stage, albuminuria is present. High colored urine with urobilinuria is often an expression of blood destruction (blood crisis) and unfavorable.

Indicanuria is of no prognostic value in pernicious anemia; it is not unusual.

Tongue.—*"Oral sepsis"* has been strongly advocated by Hunter as being of great importance and provocative of pernicious anemia; the same author believes that with relief of the septic element, the blood picture and the general condition of the patient improves. There are in some cases from the beginning marked changes in the tongue which are best considered to be inflammatory, atrophic, at times ulcerative.

Glossitis is by no means a constant attendant of pernicious anemia. In

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the late stages the shining, wrinkled, dry, often cracked and bleeding tongue is present. In all cases the tongue is pale. Marked evidences of dry tongue—the glazed, shining denuded tongue with *ulcerative gingivitis* and bleeding gums are evidences of malignancy of the anemia and indicate advanced disease.

Atrophy of the gastro-intestinal glands with glossitis and correspondingly low blood state are not often followed by long or satisfactory remissions.

Retention of the body weight, fat particularly, does not in any way influence prognosis. Cachexia is not frequent or striking. *The marked anemia is out of all proportion to the cachexia or loss of weight, while as already suggested with malignant disease, the cachexia is out of proportion to the anemia* (Henry).

Intravenous and intramuscular injections of salvarsan, intensively used have been advocated by many during the past 3 or 4 years. Personally, after a reasonably large experience with the remedy we are unable to positively say that a single case has been saved. In the graver specific anemia it does yeoman service. In those cases of pernicious anemia in which it has seemed to have a wholesome effect in stimulating the blood producing organs and improvement has resulted, there is no assurance that relapse may not follow. Indeed the improvement when it does follow is usually short-lived.

Bramwell in a recent article in which he reports his results of 21 cases treated by salvarsan and neosalvarsan had "6 without improvement (28.5 per cent); in 3 (14.2 per cent) there was slight improvement; in 5 (23.8 per cent) there was marked improvement and in 7 (33.3 per cent) there was complete (? temporary) recovery.

Ultimate results of Bramwell's series show "of 21 cases treated by salvarsan or neosalvarsan and recorded in this paper, in 1 case (4.7 per cent) the patient remains fairly well; in 5 cases (23.8 per cent) quite well; in 15 cases (71.4 per cent) the patients have died."

Such statistics are of no practical value. They are too recent and indefinite.

Bramwell correctly states the case as follows: "In order to judge fairly and accurately of its value, a series of consecutive and unselected cases, slight as well as severe, in which no other treatment has been employed, should be taken and the results compared with a series of similar cases treated by other methods."

The great majority die in coma, after a period of brain symptoms varying from two to four or more weeks. *Complications* are exceedingly rare. Occasionally *bronchopneumonia* or added *infection* causes death, not often. Pernicious anemia with atrophy of the gastric follicles and tuberculosis of the suprarenals (including bronzed skin) were found in one of our cases

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B. Leukemia

1. Leukocytic Leukemia.
   Synonyms: *Myelocytic Leukemia.*
   Splenomyelogenous Leukemia.
   Myeloid Leukemia.
   Myelemia.
   Lienal Leukemia.
2. Lymphatic Leukemia.
   Synonyms: *Lymphemia.*
   Leukocythemia.
   Chloroleukemia.
   Pseudoleukemia.
3. Acute Leukemia.
4. Leukanemia (Leube).
5. Mixed Leukemia.

1. Leukocytic or Splenomyelogenous Leukemia

The original description of leukemia with the clinical and blood pictures given by Virchow was so exact that but little which has been offered since has materially altered his original conception of the disease. Ebstein, who has made a careful investigation unhesitatingly concludes that Virchow recognized the disease before Bennett to whom the credit is usually given. The references appended make it possible for the student of medical history to study that question for himself if he desires from the literature within easy reach. Virchow did not appreciate the part played by the bone marrow until Neumann, in 1870, called attention to it. Leukemia may be defined as a condition of the blood in which the white blood corpuscles are enormously increased so as to be in the proportion of 1 to 20 of the red cells or there may be greater disproportion (1-10 or 1-5), in which there are changed relations of the normal varieties and numbers of white blood corpuscles depending on a specific cause (unknown) and irritative growth in the blood producing tissues (hyperplasia of the leukoblastic tissues) which result in the flooding of the blood with either myelocytes or lymphocytes, in accordance with the variety of leukemia present. The true nature of the disease is unknown. Some believe it resembles or is closely related to sarcoma and myeloma.

Leukocytic or Splenomyelogenous Leukemia

Blood.—The myelocytes, large mononuclear cells of Ehrlich, are in the ascendency and are supposed to differ from the large mononuclear

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lymphocyte. All blood, therefore, which contains myelocytes is abnormal. The myelocyte is normally present in the bone marrow. *In leukocytic leukemia there is an overdevelopment of the myelocytes and their casting off into the blood stream.*

Relatively the proportion of the polymorphonuclear cells is decreased. They are actually increased. There are many polymorphonuclear leukocytes, a preponderance of myelocytes, eosinophils and eosinophilic myelocytes; increased mast cells; an occasional normoblast; poikilocytes, megalocytes, microcytes, pale red blood corpuscles, and in advanced cases Charcot-Leyden crystals. The alkalinity of the blood is decreased; the specific gravity reduced (1,025-1,040); there is finally a positive reduction of hemoglobin (average early 60 per cent lower as the disease advances). Bennett characterized the disease as "suppuration of the blood."

A high myelocytic count, irrespective of the number of leukocytes is essential for the diagnosis of splenomyelogenous leukemia, just as megaloblasts are necessary for the diagnosis of pernicious anemia. The average white count in our series at the height of the disease was between 275,000 and 300,000. We have, in rapidly fatal cases made counts much higher. In one case seen many years ago with marked hemorrhagic tendencies in the terminal stage, the red and white counts during the last few weeks of life ran practically parallel—500,000 to 800,000 per c. mm. The polymorphonuclear cells average between 25 and 50 to 55 per cent; the myelocytes from 30 to 50 per cent. Almost all of our cases were without *hereditary taint*—with the male decidedly in the ascendency.

In some cases the red count may remain normal or nearly so for a considerable period, *rapid or progressive drop of erythrocytes is unfavorable, particularly if at the same time, there are evidences of increasing exhaustion, hemorrhages, purpura or increasing mental symptoms. Marked morphologic change in red corpuscles with increasing hemolysis is unfavorable for the prolongation of life.*

High fever, or even continuous elevation of temperature, slightly above 100° F. with evening rise, is evidence of advancing change and unfavorable for prolongation of life. Symptoms referable to the *nervous system* often resemble the Lichtheim complex of pernicious anemia. The greater the involvement of the nervous system the shorter is the course of the disease, as a rule. *Invasion of the sensorium* is indicative of deep toxemia or infiltrating changes in the brain and is promptly followed by death. There is greater *paresthesia* than *tabetic symptoms* though the latter may be present, also *neuritis. Tinnitus aurium* and *vertigo* are evidences of profound anemia in most cases. *Hemorrhages into the auditory system leading to deafness and uncontrollable vertigo* are unfavorable symptoms.

The *spleen* is enormously increased in size. In some cases in which, as the result of treatment or nature's processes, the white count improves, the splenomegaly shows some retraction, but this is not to be relied upon

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as occurring uniformly. In my cases treated with Röntgen Rays and Benzol, the spleen did not change in size with the improved blood picture.

Perisplenitis has not been a frequent source of pain in my cases. It has no great bearing on the progress of the disease. I have never met a death due to *rupture of the spleen* in my material, occasional cases have been reported in which rupture was the cause of death. *Marked dyspnea, cough, expectoration and physical signs of infiltration* are indications of advancing disease. *Dyspnea and cough* may be due either to leukemic infiltration of the lung or myocardium or to extreme weakness and myocardial weakness. The physical signs of *infiltration of the lung* may also be due to complicating tuberculosis. These cases all progress rapidly to a fatal issue. We consider elsewhere the influence of added *tuberculous infection* on the white blood count. *Dyspnea and respiratory embarrassment* may also be due to pressure from *hydrothorax, hydropericardium, enlarged spleen* and *liver.* The prognosis is unfavorably influenced by *gastro-intestinal complications* or symptoms. In severe cases, often in the last stage, *anorexia, vomiting* and *diarrhea, with hemorrhage,* rapidly weaken the patient.

In the terminal stages *ascites* and *general edema* are in evidence. It may happen that after the removal of the abdominal fluid toxic symptoms increase. At times life may be prolonged during a short time by such procedure. *With fibrotic and nodular changes in the liver and fatty degeneration,* or the latter alone, there may be slight jaundice. The *liver* as suggested elsewhere in this section may show *leukemic infiltration.* All of these conditions are unfavorable for the prolongation of life. *Peritonitis* is the terminal complication in rare cases.

The *urine* shows an increase of uric acid (characteristic condition); there may be moderate albuminuria, hyalin casts and evidences of acute or chronic nephritis. In some cases barring the excess of uric acid, even in severe cases, there are no changes in the urine. Occasionally the urine is of a greenish hue and Bence-Jones albumose has been present as in multiple myeloma (Kahler's Disease). Such complications are most frequent with lymphatic leukemia.

I have seen several examples of *priapism* which has persisted unrelieved by any treatment. In one woman, the clitoris was in a state of chronic erection and with vaginal irritation caused great discomfort.

The behavior of the HEART is much like pernicious anemia as the end approaches. From the beginning of symptoms there is rapid action, small and thready pulse, systolic blood pressure is low. As the disease advances the systolic force grows more and more feeble, the heart sounds embryonic and dilatation with *hemic murmurs, jugular pulsation, tricuspid insufficiency* and frequent *syncope* may precede death.

Pulmonary edema due to heart insufficiency is a cause of death. Early or late, usually late, evidences of *hemorrhagic retinitis* are in evidence with

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associated ocular subjective symptoms. Sight is not lost; optic neuritis is not frequent.

2. Lymphatic Leukemia

(*Lymphemia, Leukocythemia, Chloroleukemia, Pseudoleukemia*)

The essential features of lymphatic leukemia are changes in the lymphatic glands of the body causing multiple enlargements (increase of lymphocytic forming tissue) and the resulting lymphocytosis. The blood changes are characteristic.

Blood.—The color index is low, the hemoglobin reduced, the coagulability, alkalinity and specific gravity are much like the splenomyelogenous form. *There is true lymphemia. The small lymphocytes are in the ascendency.* There is increase in the number of polymorphonuclear leukocytes, though less than in leukocytic leukemia. The red blood corpuscles usually number 3,000,000 or below, as the disease advances. Few nucleated red cells are seen, less than in the other variety of the disease; a few myelocytes and a small fraction of eosinophils. *In both varieties of leukemia the blood platelets are increased.*

The lymphatic type shows a predilection for children and young adults, though older subjects may develop the disease. Males are more frequently afflicted than females.

The *lymphatic enlargements* may at first be limited, beginning in the neck, and extending to the axilla with, in advanced cases, multiple enlargement in the glands of the body—mediastinal, postperitoneal, mesenteric and inguinal. There are also changes in the internal organs due to infiltration.

The *spleen* may not be materially enlarged. The anemia is slower to develop in this form than with myelogenous leukemia. In some cases the *color* may remain good in spite of mulitple lymphatic enlargements. The *fever* is not likely to be an early symptom. It is often long postponed.

Skin pigmentation and *nodules* are relatively frequent. The involvement of the *oral mucosa, teeth, tonsils* and *postnasal glandular tissue,* increases septic symptoms and hastens the end.

Chloroma is a condition of lymphemia with nodules in the skull, green color of the lesions as the glandular structure proliferates, the presence of exophthalmos and facial paralysis in most cases. Chloroma may be associated with or is a part of either myelogenous or lymphatic leukemia, usually as above stated the latter. It may be associated with the acute or chronic leukemias, usually the former, but cases have been reported which lived from two to four years (Ward). The average duration of life is below seven months.

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3. Acute Leukemia (Ebstein)

Acute leukemia may be either leukocytic or lymphatic. The large majority of cases are typically lymphatic, though the splenomyelogenous form is occasionally met (Naunyn). In the latter form we have seen two cases which commenced suddenly without prodromata, with high fever following repeated chills. The spleen and liver were enlarged at once, the former was somewhat tender. One of these was a girl about 15 years of age who during several months was favorably influenced by Röntgen therapy, indeed the high leukocytic count was at once reduced and after a few weeks her physician reported counts approaching leukopenia, when her fever and chills were under control. So striking was the improvement that the case was reported at the meeting of the Medical Society of the State of New York by her attendant, who was much encouraged by the result. (Schuyler.) The improvement was short-lived. She died as did all other cases.

The typical cases of acute leukemia begin suddenly with marked febrile disturbances, the lymphatics are involved, there is lymphemia and increasing anemia. Fraenkel has reported the constant presence of abnormally large mononuclear cells, wasting and toxic symptoms, enormous prostration, hemorrhages from the mucous surfaces and purpura, (skin) and the enlarged spleen are among the symptoms.

The blood changes are exceedingly rapid. Death results in coma after a period of typhoid condition in from four weeks to three or four months. Fussell and Taylor have reported 55 cases of acute leukemia. We have never known of recovery. Cases in which there is depleting *diarrhea* die early. *Ulcerative colitis* and *enteritis* have accompanied some acute leukemias. Thymus and tonsillar infiltration, gingivitis (ulcerative) and ulceration of the buccal mucosa lead to inanition and early death. *Rapid leukemic infiltration of vital organs,* lung, liver, and kidney with skin nodules—pigmentation and leukoderma are found in both forms of acute leukemia. The more extensive the leukemic nodules, the sooner will death follow. The brain may be the seat of infiltration causing hemorrhage with resulting paralysis and other focal symptoms. *Hemiplegia* has been reported as well as ocular and aural lesions with consecutive symptoms. There are occasional cases reported in which decided increase of lymphocytes has failed to appear until within one or two weaks of death. (Litten, Waldstein, Villinger.)

The majority of acute leukemias are found in children and before the age of 20 years.

4. Leukanemia (Leube)

Leube called attention to blood changes and a clinical history in which there are evidences of myelogenous or lymphatic leukemia with grave

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anemia. The lesions present depend upon the variety of leukemia with which the grave anemia is associated. The prognosis is bad.

5. Mixed Leukemia

There are also *mixed forms of leukemia* in which the blood picture shows cellular elements characteristic of both forms of the disease.

The influence of treatment on the prognosis of all forms of leukemia has not been encouraging. Beginning with x-ray therapy and ending with benzol and mesothorium, enthusiasts have been deluded by the surprising influence of the Röntgen Ray over the long bones and spleen, and the benzol internally administered in reducing the leukocytic count. Periods of improvement of subjective symptoms have followed but we have no record at hand after wading through a large literature bearing on the subject which justifies the conclusion that a single case has been permanently benefited. *All relapse and all have died.* There is great *danger from the sudden and overpowering poisoning due to the destruction of large numbers of leukocytes following the Röntgen Ray and the use of benzol.*

The influence of *splenectomy* on leukemia is being considered, but in spite of a few reported cures (?) there are no data at hand which warrant the conclusion that the "cured" were veritable cases of the disease. Until we are better informed by experimental study on the influence of the spleen in these cases, no hope is justified by the removal of that organ. The *average duration* of life in uncomplicated cases is between six to eight months and between three and five years. My lymphatic cases have lived longer than the myelogenous.

Remissions with considerable periods of improvement are characteristic, but not so strikingly frequent as in pernicious anemia. Many splenomyelogenous leukemias are progressive from the beginning without a stay of symptoms, either subjective or objective.

Lymphatic leukemia frequently shows tendency to remain latent during long periods. Once symptoms of deep toxemia show themselves or with *purpuric* or *hemorrhagic complications, with acute exacerbations and high temperature, edema, ascites* or other evidences of *dropsy, heart degeneration,* remission cannot be expected. The subjective symptoms of all forms of leukemia have practically the same influence on the forecast.

Complications.—The influence of acute or chronic added infection upon the blood count is striking. I called attention to the influence of added tuberculosis in connection with Groat in a case of splenomyelogenous leukemia. With tuberculous infiltration of the lung and its advance, the myelocytic count was promptly reduced (Elsner and Groat, also George Dock). These observations have been confirmed by other observers in connection with a variety of complicating infections. There are but few complications. Death results from asthenia in *coma,* in most cases. *Pulmo-*

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nary edema, bronchopneumonia, exhaustion following *hemorrhages* and sudden *syncope* are among the causes of death. In all forms of leukemia the greater the number of leukemic nodules in the internal organs and skin, the more rapid is the course of the disease.

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C. Hodgkin's Disease · Lymphoblastoma

(Pseudoleukemia, Lymphadenoma, Malignant Granuloma, Adenie, Lymphogranuloma)

Hodgkin's Disease is characterized by marked enlargement of the lymphatic glands of the body, beginning, as a rule, in the cervical region and extending to distant parts (axillary, mediastinal, bronchial, mesenteric and inguinal) with more or less enlargement of the spleen and liver as the disease advances and finally the blood picture of grave secondary anemia. To sum up and contract the definition, Hodgkin's Disease may

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be considered a far-reaching disease of the organs which elaborate blood cells, including the lymphnodes, the spleen and bone marrow, which bears external resemblances to leukemia but is without the typical leukemic blood picture (Naegeli).

The disease bears close resemblance to tuberculosis without the pathologic changes which prove it to be of bacillary origin, while there are some features which resemble the leukemias, which led pathologists to name it "pseudoleukemia." *The entire history of the disease, its symptomatology and pathology create a strong suspicion of the presence of an infectious agent.* Within the last few years this suspicion has been strengthened by the experimental and pathologic researches of various men, foremost among these are Bunting and Yates who, as the result of their studies are strongly of the opinion that the *diphtheroid organism* which they have cultivated from cases of the disease in man and with which they have successfully inoculated monkeys, reproducing lesions similar to those of the disease in man, will ultimately prove its infectious nature. They say "we feel fully assured of the etiologic relationship of the diphtheroid organism (Bacterium Hodgkini) to Hodgkin's Disease." The early and tonsillar and alveolar symptoms in many cases create the further suspicion of infection and point strongly to the tonsils (teeth and mouth) as the port of entry.

Hodgkin's Disease may be accepted as a clinical entity in which the pathologic changes in the lymph glands are characteristic and include marked increase of the gland tissue, multiplication of the endothelial and reticular cells and as has been shown (Andrewes and Dorothy Reed) lymphoid cells are enormously increased and are of uniform size and shape; giant cells, the lymphadenoma cells, hold multiple nuclei; while eosinophils are constantly present. The hardness of the gland is due to the fibroid change—reticular increase. Suppuration is rare, and when this happens, there is in all probability added pyogenic infection. In some of the monkeys inoculated by Bunting and Yates, the "softening" was found, but without the presence of any added microörganism. The Bacterium Hodgkini alone grew in the cultures of these cases.

[The study of the life of Hodgkin who in 1832 described the disease which bears his name, proves him to have been one of the three clinical and pathological giants of the early half of the nineteenth century who added fame to Guy's Hospital. The other two were Addison and Bright. (Stroud, Wm.) Hodgkin deserves to be remembered not only as having made clear the clinical and pathologic characters of the disease bearing his name but as an unselfish and humane physician.]

Naegeli considers Hodgkin's Disease or pseudoleukemia a symptom complex of these diseases:

A. Lymphocytoma.—Lymphocytoma, or those in which there is proliferation which he characterizes as lymphocytic and aleukemic, in which

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the lymphatic system is largely involved, in which the spleen, bone marrow, liver or periosteum may, in individual cases present the greater changes during varying periods. Included in the lymphocytoma are:

(a) The Aleukemic Lymphadenomata (Hodgkin's Disease of most clinicians).

(b) Lymphosarcomatosis (Kundrat's Disease).

These are localized sarcomata originating in lymphatic tissue (lymph nodes usually), never disseminated beyond the lymphatic system. Liver and spleen are not enlarged.

B. Granuloma.—The granulomata are inflammatory growths and not true Hodgkin's Disease, they may be:

(a) Malignant.
(b) Tuberculous.
(c) Syphilitic.

When, therefore, we consider *"Hodgkin's Disease"* we include the *lymphocytomata* or the *aleukemic lymphadenoma.*

The course of Hodgkin's Disease may be either (a) *acute* or (b) *chronic:*

(a) *Acute Hodgkin's Disease.*—The acute form of the disease usually begins with tonsillar symptoms which resemble very closely the subjective features of acute leukemia. The advance of lymphatic invasion with associated constitutional disturbances, changes in the spleen, thymus and blood are often surprisingly rapid and ultimately fatal. In most of these cases there is fever, often marked hyperpyrexia with prompt emaciation, cachexia, and toxic symptoms (cerebral). In several of our cases, with slight enlargement of the spleen and liver, there has been edema of the extremities, purpuric spots over the body and depleting epistaxis. These cases are to be differentiated from the typical *acute or subacute relapsing cases described by Pel and Ebstein.* The *non-relapsing acute Hodgkin's Disease is always fatal and runs its course in from three weeks to as many months. The Hodgkin's process of Pel and Ebstein may continue during many months.* In this form of the disease the symptoms often resemble the more acute type but there are varying periods of relapse (7 to 14 days) after high and weakening fever, with excessive sweats, wasting and increasing secondary anemia. There may be enlargements alone of the internal glands, or as we have seen in several hospital cases, the lymphatic invasion is general and one of our cases died with mediastinal pressure of asphyxia which increased suddenly. In the Ebstein pseudoleukemia the temperature during the afebrile period may be subnormal from which there is a gradual rise to the climax. In one of our cases there was, at the beginning of each relapse, a well defined chill during which the temperature reached 104-5° F., where it

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remained much of the time for three or four days, when it fell gradually to below normal. These patients may develop *purpuric symptoms*, have hemorrhages, fall into a typhoid condition; usually have evidences of nephritis with the blood picture of secondary anemia.

Ziegler called attention to cases in which there are constitutional symptoms, elevation of temperature and increasing evidences of anemia without palpable external glandular enlargement, but involvement of the internal glands. The spleen is usually enlarged in these cases, and it has been suspected that occasionally the disease originates in the lymphatic structure of the spleen. In some cases the retroperitoneal glands alone may be involved, in others the bronchial or both thoracic and abdominal glands may be enlarged at the same time. These are considered under the head of the "*Latent type.*" We know of no recovery from a single well authenticated case of these types of the acute disease. Heffron's case presented a typical history in which mediastinal pressure promptly caused death. Such cases are not infrequent. For the full study of the symptomatology of the relapsing type of Pel-Ebstein the reader is referred to McNally's paper (See References).

(b) *Chronic Hodgkin's Disease.*—The onward march of the disease is slow, the first evidences are the enlargement of the cervical glands, usually one sided, at the angle of the jaw. The extension to the opposite side may be long postponed but careful examination in most cases will detect an abnormal hardness and some enlargement of one or more deep cervical glands long before the growth extends to the other side of the neck. The enlargement of the lymphatics may be surprisingly extensive as the disease advances and multiple skin nodules are not uncommon. A recent case showed extensive *bronzing of the skin*—probable involvement of the suprarenals. This man in spite of the existence of the disease during several years (3) and glandular enlargements in all possible directions, palpable spleen and liver, with a blood count with all the characteristics of moderate secondary anemia and albuminuria, was able to work his farm and walked without discomfort.

When the *mediastinal glands* are involved the pressure symptoms are persistent and increase; the suffering is acute and with edema of the face and arms, or at times with only symptoms of compression death promptly follows.

The *blood picture* is not pathognomonic. As already intimated Hodgkin's Disease in the chronic type leads to blood changes which correspond with those of secondary anemia (anemia gravis). There are cases in which the glandular enlargements are prominent without discoverable changes in the blood. These are among the most chronic cases; life is not threatened during long periods unless death is caused by pressure or other complications. In the average case the leukocytic count is not markedly increased. Even in the acute cases this rule holds and

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makes differential diagnosis easy. In some, particularly during febrile exacerbations, there is moderate leukocytosis (10,000-30,000). Lymphocytes may be increased with the fall of polymorphonuclear cells. In these cases they may represent 75 per cent of all white cells. Pinkus holds that the *relative lymphocytosis* is typical of the disease. Bunting believes that the diagnosis can "be made with a considerable degree of accuracy" from the blood picture, and does not agree with Pinkus that lymphocytosis is typical. It may be safely concluded that the more chronic and serious cases show the greater changes in the blood, anemia and some leukocytosis. The "two constant features" which Bunting holds for diagnosis and therefore for prognostic data, "an increase in blood platelets and an absolute increase in the transitional leukocytes," cannot be accepted in all cases. We are agreed that the majority of late cases show marked neutrophilic leukocytosis "and a diminution in percentage of all other elements except the transitional leukocyte."

There are cases (Naegeli and Baumler) in which the lymphocytes are markedly reduced with marked neutrophilic leukocytosis, eosinophilia and increase of mast cells. With the cases which have been characterized as "*infectious granuloma*" the neutrophils continue normal and the lymphocytes are much decreased.

Yates who has collaborated with Bunting makes the following statement, "In spite of Dr. Bunting's work, on the blood picture of Hodgkin's Disease, it is almost universally accepted that there is manifested herein, nothing essentially or constantly characteristic." In the chronic cases without marked change in the size of the enlarged glands there may be decided *remissions*. In rare cases the glands appear somewhat reduced, that may have been imaginary. The remission may be due to an improvement of the periadenitis which is present in some cases.

The remissions are not as oft repeated or as long as in pernicious anemia. During periods of remission the appetite improves, the general condition is better and patients are often able to continue at their work.

Relapse is the fate of all and progression to a fatal termination.

The *duration* of the chronic cases varies. The average of our cases was in the neighborhood of three years. We have seen cases which lived much longer, one, the longest of our series lived over seven years. Morawitz reports the possibility of the extension of life beyond ten years in some cases.

There is in almost all chronic cases a period which Trousseau characterized as the "*periode latente*," this with glandular enlargement and no constitutional symptoms may continue during surprisingly long periods; one to three years are the extremes. The "*period progressive*" is variable; once the symptoms and lesions are prominent and are progressive there is not much hope of long periods of remission. The final "*periode cachectique*" of Trousseau is coincident with the terminal stage

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and from this there is no release. The symptoms of the cachexia are the pallor, weakness, low red blood count, dyspnea, albuminuria, hemorrhages and purpuric skin changes, bronzing and nodes in the skin, increase of persistent fever, marked enlargements of the spleen and liver, ascites, edema of the extremities, and a period of toxic nervous (brain) symptoms, with small, thready pulse, hemic murmurs, jugular pulsation and tricuspid insufficiency (relative) at times.

Hemorrhagic symptoms are rarely present early; *petechiae* with or without large hemorrhages from mucous surfaces are ominous. The *transition of an original pseudoleukemia to leukemia is possible and occasionally happens.* In rare chronic, as in the acute cases, limited lesions—localized forms of the disease may offer but few or indefinite symptoms during long periods; thus the disease may begin in the mesenteric or postperitoneal glands, be followed by *latent periods;* extension is sure to follow.

The *leading causes of death* are toxemia, exhaustion, pressure and added infection.

Tuberculosis is rarely a complication.

The *surgical treatment of Hodgkin's Disease* has in my experience been absolutely unsuccessful. On the other hand, it has often seemed to stimulate the growth with extension of lymphatic enlargement. Able clinicians believe that in some cases the progress is halted by early removal. No form of treatment—x-ray, surgery, vaccine, serum, drugs, climatic or hygienic, has so far as we have been able to discover, saved a single life. In making the foregoing statement, we are not unmindful of the reported experiences of Yates, who in concluding his article says ". . . even these few cases indicate that primarily Hodgkin's Disease is a localized process, susceptible of cure when properly treated as a malign, though chronic infection. It may persist for years without manifesting itself save in the blood picture so that cures may not be assumed until after an uninterrupted duration of years of persistently normal conditions."

Syphilitic granuloma offers a favorable prognosis. This is not a true Hodgkin's process nor are any of the granulomata to be so considered. (See Naegeli's Classification in this article.) The inflammatory and tuberculous granulomata offer an unfavorable forecast.

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D. Purpura

Hemorrhagic Diathesis

In considering the prognosis of the *symptom complex of purpura* we adhere to the following classification which is based upon the hypothesis that the *hemorrhagic diathesis* includes a variety of symptoms of a large number of heterogeneous diseases (Naegeli) and further that all so-called *"primary purpuras"* including simple purpura and purpura hemorrhagica, acute or chronic, are all identical, they simply differ from each other in degree and intensity of constitutional symptoms.

Classification

- Purpura
  - 1. Secondary.
  - 2. Primary
    - (a) Simplex.
    - (b) Rheumatica (Schoenlein's disease).
    - (c) Hemorrhagica (Werlhof's disease) (Morbus maculosus Werlhofi).
    - (d) Chronic purpura.
    - (e) Henoch's purpura.
    - (f) Hemophilia.

1. Secondary Purpura

Secondary purpura as we have demonstrated repeatedly in this work is an expression of a septic or toxic process; *symptomatic* always of one of many constitutional disturbances and may include scorbutus, hemophilia or the hemorrhagic diathesis. Among the leading conditions with which purpura may be associated are the leukemias, pernicious anemia, Hodgkin's lymphadenoma, malignant endocarditis, carcinoma, sarcoma, the infections (usually the more severe), vasomotor disturbances associated with nervous disorders, tabes dorsalis, myelitis and hysteria, all cachexias from

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whatever cause and the various intoxications from drugs or other sources (Ergot, belladonna, mercury, iodin and snake bites). Purpura in those with a strong diathesis may follow *mechanical insult.*

Classifying the above causes of secondary purpura into separate groups we find them to be *infectious, toxic, cachectic, neurotic* and *mechanical.* (Osler.) The forecast of secondary purpura always depends upon the malignancy or nature of the underlying cause. In all of these conditions the addition of purpura may, if it is extensive, unfavorably influence the progress of the disease, but it should rather be interpreted as an expression of a grave infection or disturbance.

(The reader is referred to the separate diseases of which purpura is a symptom for fuller data.)

Hemorrhagic scarlet fever and smallpox are examples of malignant infection associated with secondary purpura. Erysipelas offers another example.

It may be safely concluded that the *grave infections which are "hemorrhagic" (purpuric) at their height, always offer a grave prognosis. This is not always true of purpura which follows the infections, either shortly after the acute symptoms have subsided or later.*

Severe bleeding from many surfaces may follow typhoid fever and the patient may show marked depletion, secondary anemia. Nevertheless, recovery is the rule under favorable surroundings and rational treatment. The larger hemorrhages with the anemias and leukemias weaken the patient and hasten the course of the disease.

With cancer and sarcoma, purpura is almost always included among the terminal symptoms. With myelitis, tabes dorsalis, cerebrospinal meningitis and the depleted neglected alcoholic, the downward course is promptly evident after the advent of purpura. Extensive ecchymosis of the genitals in tabetics is a late symptom in the more reduced subjects. In children the administration of iodin in any form (we have found it after even small and continuous doses of syrup of the hydroiodic acid) may cause purpura, hematuria usually, and threatening anemia. With the discontinuance of the drug and proper care, the child in the absence of serious primary disease recovers. In the adult with decided hemorrhagic diathesis iodin in small or large doses may cause hemorrhagic purpura.

2. Primary Purpura

(*a*) *Purpura Simplex*

Simple hemorrhage into the skin, without known cause, may be limited or universal and may develop at any age. It is usually found in early life. It is often an expression of reduced vitality and resistance. The malaise anorexia, and (occasional) slight fever which accompanies it, with at times acceleration of the pulse may precede the petechiae several

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days, making positive diagnosis impossible. The subjective symptoms fade in from 3 to 7 days; the hemorrhagic spots show the characteristic changes in color after from 4 to 8 days and appear ecchymotic during two weeks or more. Often these "black and blue" spots persist longer. Purpura simplex bears all of the earmarks of a mild infection from which recovery without complication is the rule without sequelae.

The *blood picture* in most simple purpuras is not materially changed. Occasionally there is a reduction of eosinophils—with convalescence these are promptly increased to the normal. *Diarrhea,* which is an occasional symptom is easily controlled and is never severe.

Purpura fulminans is a malignant type of simple purpura which develops in young infants (3 to 6 weeks old) without known cause, without hemorrhages from the mucous surfaces but with large hemorrhages into the skin, either limited to one extremity or both, or universally spread, with swelling of the parts, deep sepsis and death in from 2 to 7 days.

(*b*) *Purpura rheumatica*

Schoenlein's Disease

We have found purpura rheumatica,

1*st*, with symptoms referable to one or more joints (usually the ankles) during several days, without known cause, with but little constitutional disturbance, followed usually on the third or fourth day, sometimes earlier, at times later, by petechiae confined as a rule to the skin below the knees, either few or many. In six to ten days the disease ends favorably. The pain is likely to be more or less relieved as the eruption appears. Recovery is complete and without incident.

2*nd:* Cases in which with the joint tenderness there are evidences of mild tonsillitis, more or less febrile movement and finally the same behavior of the petechiae as in the preceding cases. These patients do not convalesce as rapidly as do those without tonsillar symptoms, and there is often a strong suspicion of an underlying grave infection. Cases with exactly parallel early histories have been found to develop endocarditis and in rare cases the petechiae have proved to be due to malignant endocarditis. The majority of these cases, however, are benign and recover without permanent damage.

3*rd:* There is a variety of purpura rheumatica which so closely resembles *erythema nodosum* as to lead us to the conclusion that the latter condition is but another form of purpura, dependent upon some unknown infection. In these cases the nodes—tender and erythematous—with in some, limited evidences of petechiae follow. A few days of tender or stiff joints, or without joint symptoms; only the pains due to the presence of the nodes and "stiff legs" follow. The ecchymosis persists several weeks, the nodes gradually disappear with full return to health. In children

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(2 to 8 years or older) the course is shorter than in the adult. There is a tendency to recurrence or a subacute course in some of the adult cases. Life is never threatened and full recovery may be expected.

Recurrence is more likely with all forms of "rheumatic" than with the simple purpura.

(c) *Purpura hemorrhagica*

(*Morbus maculosus Werlhofi*)

Werlhof's Disease is associated with hemorrhages from one or more mucous membranes with the usual dermal bleeding of purpura simplex in most cases. This is the gravest form of purpura, for in individual cases bleeding from many surfaces or into vital organs (brain) may threaten life. Hemorrhages from the nose, kidney, intestine, bladder, or bronchial mucosa may promptly deplete the weak subjects who are most predisposed to the disease. It occasionally happens that hemorrhage into the brain substance causes *hemiplegia;* into the brain membranes hemorrhagic meningitis. The *purpura fulminans of the adult* is an example of this form of so-called primary purpura. In such cases previously healthy subjects are suddenly seized, hemorrhages from several mucous membranes are coincident, septic symptoms promptly develop and death may follow within the first or second week. I have elsewhere in this chapter mentioned the *purpura fulminans* of early life, in which the symptoms as a rule, do not include bleeding from the mucous surfaces and justify its classification as a malignant type of purpura simplex of early life.

The blood picture of Werlhof's disease is that of secondary anemia. In the graver cases the blood clot does not contract, if it does, the coagulation is slow, and the blood platelets are markedly diminished (normal 250,000 to 400,000 per c. mm.). The lower the red count and color index the longer the convalescence and the graver the prognosis. The prognosis of Werlhof's disease is now materially and favorably influenced by the prompt use of the animal serum after the method which prevents anaphylaxis and which we have recommended (Elsner and Meader) for the treatment of the chronic forms of the disease. In the adult fulminating purpura, the prognosis has been materially improved by the introduction of animal serum (preferably rabbit serum). Morbus Werlhofi may, because of *hemorrhage into the appendix* cause symptoms of appendicitis. One such case I had in my practice where the appendicular symptoms were the first and simulated appendicitis; the appendix was removed, was hemorrhagic, in two days other hemorrhages followed from mucous surfaces, and the significance of the hemorrhagic appendix was cleared. The patient made a perfect recovery without recurrence of symptoms. Uncomplicated Werlhof's disease which is not of the fulminating type usually leads, after slow convalescence to permanent re-

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covery. Our experiences with the graver types of the disease with modern treatment have been exceedingly encouraging.

In offering the forecast in any case of threatening purpura it is safe to conclude that the changes from hemorrhage, barring cerebral apoplexy, are insignificant compared with those of complicating nephritis.

(*d*) *Chronic Purpura*

Chronic purpura has received but scant attention from writers on internal medicine, yet it is a complex which is not infrequent. The clinical picture is kaleidoscopic and the cycles of the disease include repeated recurrences of all classified types of the disease in the individual case.

In the chronic cases, with a simple purpura, there may be a prompt addition of the rheumatic form, and while this seems in the ascendency, the hemorrhagic nature of the disease may be emphasized by drains from one or more mucous surfaces, occasionally hemorrhage into the brain or into hollow or solid viscera. Besides this, chronic purpura may alternate with *erythema multiforme* as we found in one of our cases (Elsner and Meader). Two or more forms of purpura may be present and persist with varying intensity during limited periods at the same time.

In rare cases (one of which we have reported) whether because of embolic infarct, thrombosis or necrobiosis, due to some other unknown pathologic cause, death of the hemorrhagic skin results.

Chronic purpura is exceedingly rebellious to ordinary treatment—repeated relapse is the fate of almost all. Two of our cases cover a period of twelve and fourteen years respectively. Osler mentions a case which was purpuric 36 years and Halsted operated on a case of cancer in which the patient had been purpuric since childhood. Bensaud and Rivet give the most complete résumé of this subject. They report cases "with periods of quiescence, during which the return to apparent health seemed complete, but the phenomena recurred on extreme fatigue."

There are two forms:

(1) the *continuous* and (2) the *intermittent.*

1. The *continuous form* is associated with general debility, rheumatism and gastro-intestinal symptoms. Ecchymoses come and go during many years; the individual petechial spot disappears promptly. Epistaxis and gingival hemorrhages are frequent. There are always some evidences of purpura present but without the greater accidents which characterize the free crises of other forms of purpura hemorrhagica.

2. The *intermittent form* of chronic purpura is more frequent than the continuous. In the crises there are "abortive and anomalous phenomena." Crises may be preceded for months or years by frequent isolated

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hemorrhages, nasal and gastric. The exacerbations are in no way distinguishable from Werlhof's disease. Slight fever may be present. Between attacks the patient usually appears absolutely normal. Slight cause produces prodromal symptoms which are promptly followed by hemorrhages. *Recurrences* have been observed covering periods of over 20 years. *Intermediary periods* may be long—seven—eight and in one case seventeen years.

The mode of termination is variable. Long latent periods do not justify the conclusion that the patient is cured. Patients may die during a crisis. The disease cannot be considered benign. *Hemorrhage is the cardinal symptom of all types of chronic purpura.*

The *blood picture* shows secondary anemia while the blood clot does not contract, the coagulation time is normal and the blood platelets are diminished. The increase of blood platelets is favorable. The results of treatment with rabbit serum (*preventing anaphylaxis*) is encouraging, and while not all are permanently cured, symptoms are promptly controlled and long periods of latency may be expected to follow. The improvement is often surprisingly prompt. In the chronic cases the animal serum is a life saving remedy. (Elsner & Meader.) In all grave purpuras the absence of regenerative forms (nucleated red corpuscles) argues against a favorable prognosis. Thayer holds that hypoleukocytosis in the acute anemia is unfavorable as is also "the greatly increased percentage of small mononuclear elements."

(*e*) *Henoch's Purpura* (*1874*)

Henoch's purpura is a variety which may be associated with urticaria or erythema, with symptoms referable to the gastro-intestinal tract more or less toxemia and albuminuria very often. This variety was originally described by Henoch and considered clinically by Osler. The *visceral symptoms* include gastric, splenic and nephritic disturbance. The gastric and intestinal symptoms often arise suddenly, are suggestive of *appendicitis, intestinal hemorrhage* may be present and due to intussusception, vomiting and colic are frequent. My most serious cases have shown positive evidences in the urine of *nephritis.* The *spleen* is enlarged and edema is not unusual. It is a doubtful question whether Henoch's purpura is a primary disease, whether it is not due to intestinal infection or whether uremia is not responsible at times. When the complex is associated with chronic nephritis it usually leads to death.

Henoch's purpura is in reality erythematous although with increasing intestinal and visceral symptoms there may be petechiae. The complex is liable to recur and is usually found in children. The prognosis is good in almost all cases which are not burdened by serious complications (nephritis, etc.).

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(*f*) *Hemophilia*

Hemophilia is an expression of the hemorrhagic diathesis which is congenital, hereditary and permanent. It attacks the male members of families of "bleeders" and is transmitted by the female offspring of these to following generations. Females remain unaffected. They do not bleed, though their male offspring shows the classic features of the disease early in life. These "bleeders" continue to bleed during abnormally long periods when they prick or cut themselves or after any mechanical insult. The cutting of the umbilical cord, circumcision, the eruption of a tooth or extraction may prove the hemorrhagic diathesis. In some, the bleeding may not occur until varying periods following birth. There are enormous variations in the symptomatology of hemophilia. Some "bleeders" may never bleed but once, others bleed on slight cause, learn their tendency and with caution live to ripe old age. If the hemophilic lives beyond puberty the chances are that his life will not be shortened. With increasing years the chances of bleeding are reduced. The serious cases are likely to die during early childhood. There are no clinical anomalies which are characteristic of hemophilics. Those whom we have seen, who continued to bleed during adult life were anemic (chloranemia).

The blood picture offers nothing characteristic. The coagulation time is reduced in hemophylics and is deficient. There is no organ which may not bleed; bleeding from mucous membranes is the most frequent cause of depletion. These include epistaxis, hematemesis, hemoptysis, intestinal hemorrhage, renal, vesical, and bleeding from ulcerated gums (ulcerative stomatitis and gingivitis).

Pyorrhea alveolaris frequently retards the progress of hemophilics. *Petechiae* or *large surface hemorrhages* may arise suddenly but are more limited usually than with other forms of purpura. *Joint hemorrhages* are usually absorbed, permanent damage may occasionally follow (Erosion, anchylosis and contracture) usually there are no permanent lesions. The knee is the most frequent seat of hemorrhage.

In individual cases the bleeding may continue during exacerbations from only one organ, as the kidney or bladder, nose, stomach or intestines. Senator's case has become famous in which a bleeding kidney removed from a hemophilic girl, aged 19 years, was found normal, but she never had recurrence of hemorrhage.

Hemophilia is not limited to any one portion of the world, it is rare but is universally distributed. Grandidier gathered the records of 93 hemophilic families in Germany with 258 bleeders of which 22 were women. Bullock and Fildes in their report give a full bibliography of the subject. Morawitz reports the family Mampel which has been observed at Kirchheim near Heidelberg since 1827 and since that time has never been free from bleeders.

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E. Erythremia

1. Primary Erythremia

(*Osler's Disease, Vaquez Disease, Polycythemia vera, Plethora vera*)

Osler's Disease is characterized by an excess of red blood corpuscles, an increase in the volume of the blood, the subjective appearances of plethora, with enlargement of the spleen and in all likelihood a lesion of the bone marrow in which the erythroblastic elements are primarily involved. With primary polycythemia there may or may not be *cyanosis*. True erythremia exists without known cause. It is a disease of adult life (30-50 years). The prominent and cardinal symptoms of *plethora vera*, as the disease is sometimes named, are the increased number of red blood corpuscles, increased volume of the blood, increased viscosity, the plethoric appearance of the patient and the enlargement of the spleen. Barring the enlargement of the spleen, the blood features of primary and secondary erythremia are practically identical. The striking appearance of the patient at once creates the suspicion of the disease; the blood count is confirmatory, the cautious physical examination must decide whether the condition is primary or secondary.

In my last case I never found the red count below 8,000,000 per c. mm. Much higher counts are recorded. The characteristic color of the face is not materially changed in these subjects by any known treatment.

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After venesection there may be less plethora but soon the regenerative process is stimulated and the features of the disease return.

The *enlargement of the spleen* is never so great as in leukocytic leukemia. When the spleen is enormously enlarged it may be positively concluded that there is some complication. In a few authentic cases the liver has been found slightly enlarged.

Destruction of large numbers of red blood corpuscles may lead to hemoglobinuria—a dark urine with urobilin. The disease is progressive, there is marked tendency to arterial *degeneration* (arteriosclerosis) and in some cases *hypertension* is prominent. Polycythemia as it advances may finally lead to *dilatation of the heart and degenerative changes of the myocardium.* These conditions with dropsies (edema, ascites, hydrothorax) are associated with albuminuria and are evidences of the terminal stage of the disease.

Uhthoff has reported purpuric symptoms in some of his cases. He found bleeding from the gums, stomach and intestines after which his patients were materially relieved.

Erythromelalgia has been noted by several continental observers (Türk, Weintraud and others). When subjective symptoms are in the ascendency and persist, it may be assumed that the disease is progressing. The most *unfavorable subjective symptoms* are *extreme fatigue, vertigo* of the Meniere type (Naegeli), *vomiting, somnolence* and *dyspnea on* slight exertion. *Albuminuria* per se, without positive evidences of nephritis is usual and without decided prognostic significance.

Persistent abdominal pain is an early symptom, usually recurrent and not of importance. These patients are usually obstinately constipated. There are *atypical cases,* in all of which, however, there is *erythrocytosis.* Geisbock's *polycythemia hypertonica* is without perceptible enlargement of the spleen but with abnormally high systolic blood pressure. Morris has reported cases in which there was slight enlargement of the spleen but no polycythemia. Naegeli does not accept these as true erythremia.

Blood Picture.—*Erythrocytes.*—The average count in plethora vera ought not to be below 7,000,000 per c. mm. and may reach to 10 millions or higher. Osler reports 11,600,000, Stern 13,800,000 per c. mm.

Hemoglobin averages between 100-140. Rosengart reports 190-200. *Color index* is surprising low. The individual cells are pale. The *relative leukocytic count* is not materially disturbed. There is usually a slight leukocytosis. In severe cases the leukocytes may suddenly or gradually increase. Osler reports one case in which there were 91,000 with 93.2 per cent of neutrophilic leukocytes.

Eosinophilia is present in most cases, while *mast cells* are according to most observers constantly present and strikingly increased (Morris, Müller). The entire quantity of circulating blood is increased as is its viscosity and specific gravity. The disease is insidious in its onset, is

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progressive, exceedingly chronic, the patient living many years in fair health. It is practically uninfluenced by medicines, save free catharsis. Diet has a wholesome effect in relieving some temporarily while repeated venesection often relieves subjective symptoms. Osler's disease is incurable, death may result from secondary complications, usually from dilated and insufficient heart with general dropsy including ascites. Hemorrhage into the brain or its membranes; thrombosis and infarct, invading the spleen are causes of death. Polycythemic patients when they contract infection or are subjected to extra strain are found below par and without the resistance to withstand serious disease. Convalescence from insignificant complications is abnormally slow.*

2. Secondary Erythremia

(*Symptomatic Polycythemia*)

Secondary polycythemia may be symptomatic of any disease in which the blood is concentrated, in which there may be stasis due to circulatory obstruction or in which the lungs have not accommodated themselves to changed altitude or in which, because of poisoning, coal gas or drugs, as potassium chlorate, phosphorus, coal tar products, sulphuretted hydrogen, (*methemoglobinemia* and *sulphemoglobinemia*) blood changes follow.

The leading primary diseases which lead to *symptomatic plethora* are chronic heart diseases, congenital heart defects, emphysema with right heart involvement, obstructive lung, laryngeal and bronchial disease, any disease causing chronic dyspnea, diabetes mellitus and insipidus, Asiatic cholera, depleting diarrhea and high altitude, besides the poisons mentioned in the preceding paragraph.

The prognosis of all of these conditions must be separately considered; polycythemia—the symptom—is an expression of added gravity in most chronic heart diseases and congenital defects and influences prognosis as such. It is surprising on the other hand to find with congenital heart lesions and many chronic diseases how comfortable the cyanosed and polycythemic subject remains during years, but how ready he is to yield to slight cause. In such cases the primary lesion is the cause of death, the erythremia is a condition which can never be credited with paramount significance.

Parkes Weber in an interesting article on the Prognostic Significance of Secondary Polycythemia in Cardiopulmonary Cases makes the following statement:

"Just as hypertrophy of the walls of the heart is useful in so far as it

* (Besides Osler's classic article which placed the disease upon a scientific basis and gave it the name it now bears, Senator's monograph is most instructive.) (See References.)

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compensates for mechanical defects in the valvular apparatus, so also is polycythemia useful in so far as it compensates for difficulties in the proper oxygenation of the blood and tissues of the body; but just as in cardiac valvular disease great hypertrophy of the heart indicates some grave defect in the valvular mechanism, so also an extreme increase in the number of erythrocytes in the blood points to there being great impairment of the normal process of oxygenation of the body." With the "cardiopulmonary cases," however, with which I am chiefly concerned in the present paper, the prognostic significance of the polycythemia is, I believe, somewhat different, or rather, as I would prefer to put it, the outlook is exceedingly grave at the stage of the disease when cyanosis and a great degree of polycythemia become striking clinical features.

With *diabetes* we have noted the secondary polycythemia in the more serious forms of the disease, usually most marked in advanced cases (See Diabetes Mellitus).

The *polycythemia following change to a high altitude* is transitory in normal subjects and usually yields without permanent damage. Polycythemia due to chronic poisoning yields in most cases to discontinuance, though with acute poisoning it is always an expression of the gravity of its cause. The *blood picture* of secondary polycythemia is much like that of Osler's disease, unless as sometimes happens the primary lesions may produce changes. Thus with pneumonia or acute infections, with Asiatic cholera, the leukocytic count will be markedly influenced. The *polycythemia neonatorum* is physiologic and transitory.

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Section V

Diseases of the Digestive Apparatus

A. Diseases of the Mouth

Stomatitis *

(*a*) *Simple Catarrhal or Erythematous Stomatitis*

Stomatitis or acute inflammation of the mouth may be due to:

1. "Chemical or mechanical irritation including acids, alkalis, tobacco and highly seasoned food."
2. "Chronic poisoning by mercury, arsenic or lead."
3. "Extension of inflammation from the neighboring parts, e. g., teeth, nose, nasopharynx."
4. "Gastro-intestinal disturbances."
5. "Constitutional disturbances, e. g., measles, variola, scurvy." (Woodwark.)

In mild cases the affection is limited to the gums; in the more severe to the buccal mucosa, the tongue and the lips. There are no marked general disturbances though children and susceptible adults have slight elevation of temperature. The sublingual and submaxillary glands are often swollen. The course of the disease is short, cure follows in the average uncomplicated case soon after the removal of the cause. With the infections the dryness of the mouth and salivation with local swelling of the mucosa and glands promptly disappear with recovery.

(*b*) *Aphthous Stomatitis*

Aphthous stomatitis is more severe than the simple, there is a patchy (gray) deposit on the lips, gums and tongue, with considerable glandular swelling and with the disappearance of the grayish, fibrinous deposit,

* The surgical conditions are not treated in this work, neither are the surgical diseases of the nares, postnasal space or tongue.

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superficial but painful ulcers remain, which with cautious cleanliness heal in the course of four to seven or ten days. The aphthous deposit may cause multiple ulcerations of the buccal mucosa, the tongue, lips, and gums; the glands may be tender, suppuration is exceedingly rare. With added gingivitis, the teeth are at times loosened but are not lost. The inability to take food, particularly in young children, who are oftenest affiicted, may lead to weakness but to nothing more serious. We have seen children and adults in whom the disease has extended to the pharynx, the tonsils and tonsillar pillars who have finally shown few superficial deposits and ulcerations, which have promptly healed, though progress has been retarded by the extension.

The epidemic form of aphthous stomatitis is separately considered (See Foot and Mouth Disease).

(c) *Ulcerative Stomatitis*

Ulcerative stomatitis may be either *primary* or *secondary*. The secondary forms are associated with the diseases of childhood, including scarlet fever and other infections elsewhere considered. The prognosis depends on the virulence of the primary infection.

Primary ulcerative stomatitis is unquestionably of infectious character. In the severe forms fever and rapid, at times erratic, pulse (arhythmia) may accompany ulcerations of the buccal mucosa, the gums, lips and tongue. There is a characteristic odor, glandular enlargement. In children and adults many may contract the disease from the same drinking cup. In adults there is always a justified suspicion of mercury as the cause which demands investigation.

The mouth may infect itself from the neglect of the teeth. In rare cases the infection causes an erythematous eruption which creates the suspicion of scarlatina. The ulceration and swelling with foul breath not only rob the patient of appetite but make swallowing and mastication exceedingly painful. We have never known of a death in our experience, though young and feeble children (infants) are reported to have died of the disease. The duration averages two weeks. Non-infectious (?) and limited ulcerations of the mouth in both children and adults heal readily. In some there is a strong tendency to recurrence. *Cankers of the mouth* may often prove exceedingly painful and their recurrence at short periods or the constant presence of one or more may make the patient wretched. Such cases are dependent upon an underlying cause which demands close investigation. When discovered (often difficult) recovery follows.

Jacobi described an *herpetiform stomatitis* which he has found in neurotic individuals and characterized it *stomatitis neurotica chronica*. It is

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exceedingly rebellious to treatment. Osler says "it may precede or accompany the fatal forms of *pemphigus vegetans.*"

The Plaut-Vincent angina, infection from the fusiform bacillus, may limit its ravages to the gums. It is not without danger when widespread. (See Vincent's Angina.)

Leukoplakia Buccalis, buccal psoriasis—leukokeratosis mucosae oris is a condition of "*patchy tongue*"—the roof of the mouth, gums, lips and cheeks may be spotted, with whitish, grayish thickenings in patches, the tongue may be uneven or "wrinkled"; the tissue involved may become fissured. *Epithelioma* may develop after long periods of chronicity. The condition is always secondary, found in smokers usually; it is of syphilitic origin with but few exceptions. We have never seen a case in adult life which could not be traced to syphilis. Cure of the local lesion is the exception. It does not interfere with life save as cancer develops.

Oral Sepsis (Hunter).—See Pernicious Anemia.

Foul or fetid breath is always secondary, due either to disease of the teeth, pyorrhea alveolaris, tonsillar deposits, usually millet-seed sized, in the crypts of the tonsils, diseases of the stomach, sudden inhibition of digestion after emotion or shock or nasal disease. Foul breath is often rebellious to treatment but persistence after the recognition of the cause leads to cure.

The *causative relations of stomatitis*—gingivitis—and pyorrhea alveolaris to the arthritides and other infections are separately considered (See Rheumatoid Arthritis—Chronic Rheumatism, etc.).

(*d*) *Noma—Cancrum oris—Gangrenous Stomatitis, Wasserkrebs* (*German*)

Noma was described by the older writers on medicine as afflicting many and after rapid progress with gangrenous destruction of the cheek (one or both) with all of the features of overpowering sepsis, these unfortunates usually died. At present we rarely see characteristic noma or cancrum oris. Our entire experience is limited to two cases. One of a young lady aged about 28 years who developed the disease after biting her cheek, the constitutional evidences of sepsis were present early, the gangrenous destruction was prompt and death followed in ten days in *coma with albuminuria and casts.* The odor was characteristic of gangrene and the suffering intense until she became unconscious. As a rule there is little pain. Our second case was in a child in whom the process was rapid with deep sloughing of one cheek within three days and death with all of the earmarks of general sepsis about the sixth day. Kindborg reports *aspiration pneumonia* as a cause of death and he believes that noma never develops in a normal mucosa.

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The milder cases recover; those with deep sepsis, far-reaching gangrene without resistance and of tender age die. Adults may develop the more malignant type and die before the end of the tenth day.

High temperature, rapid, erratic and small pulse with evidences of *toxic nephritis* are all unfavorable, when together recovery is not to be expected.

(e) *Stomatitis Parasitica—Thrush-Soor—Muguet*

Thrush in healthy children and adults is an insignificant infection, dependent upon the *oidium albicans.* Its favorite seat is in the changed or diseased mucosa. Most cases may be traced to carelessness, uncleanliness of bottles, nipples or utensils. The disease is preventable. In children and healthy adults recovery is prompt. There are cases of tuberculosis, carcinoma of the stomach, pernicious anemia and diabetes (the latter very often in the terminal stage) which are unfavorably influenced by the development of this form of stomatitis. There is always in neglected or cachectic cases danger of spread to the esophagus, stomach and intestines. When there is extension to the intestines *obstinate diarrhea* is often depleting.

(f) *Mercurial Stomatitis—Ptyalism*

Stomatitis with salivation following the administration of mercury or the use of mercury in the various occupations offers a favorable prognosis, though it often resists treatment during many weeks and may cause ulcerative changes from which recovery is also slow. Even small doses of mercury in some in whom the usual cautions have been neglected may lead to *ptyalism.* We have seen patients much reduced by uncontrollable *salivation* and extreme weakness has followed in some cases, but recovery in the average case is the rule in from two to three weeks. Marked anemia and slight albuminuria disappear with the relief of local symptoms and convalescence is rapid. In children the development of the teeth or the decay of those already erupted is not unusual.

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B. Diseases of the Salivary Glands

1. Mumps

Epidemic Parotitis

(See Section I, The Infectious Diseases.)

2. Parotitis

The symptomatic parotitides are considered with the primary diseases which they complicate. (See Typhoid, Pyemia and other Infections.)

Chronic parotitis is almost always a secondary disease associated with nephritis, syphilis or it is due to chronic poisoning, lead, mercury or iodin.

3. Mikulicz's Disease

(*Bilateral Salivary Swellings*)

Mikulicz's Disease (1888 and 1892) is a coincident enlargement of the parotid, lacrimal and buccal glands which is chronic, continuing many years and is of uncertain origin. In America the disease is rare, though several cases have been reported. The organic changes in the glands usually persist in spite of treatment. Osler reports the case of a girl of eleven, with enlarged spleen, death resulted from chronic tuberculosis and "before death the enlargement of the salivary glands had disappeared—the lacrimal glands were completely sclerotic."

A recent article by Thursfield calls attention to the cases "which illustrate all stages of gradation between the strict type (cases with involvement of the lacrimal and salivary glands without changes in the lymphatic glands and in the blood) and those in which there is a positive picture of leukemia or lymphosarcoma.

It is possible for cases which originally show the characteristic coincident enlargement of the parotid, lacrimal and buccal glands, to develop grave blood changes and present in the terminal stages, with grave anemias, more particularly leukemia. In these cases many lymph nodes are enlarged throughout the body and there are organic changes in the spleen. Most of these cases retain the bilateral swelling of the salivary glands.

Brunn's classification, in which the "Mikulicz symptom complex" was the leading feature and which must serve to prove the association of grave blood changes in a number of cases also corroborate the conclusions of Senator, Stock, Dunn and Thursfield, that the complex may be a phenomenon of leukemia.

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Brun's classification follows:

"I. Cases without alterations in the blood.

A. Without swelling of the spleen or lymphatic glands.

(a) Symmetrical swelling of the lacrimal and salivary glands.

(b) Symmetrical swelling of the lacrimal glands alone.

(c) Symmetrical swelling of the salivary glands alone.

B. With swelling of the spleen or lymphatic glands.

(a) Symmetrical swelling of the lacrimal and salivary glands.

(b) The same with infiltrations of the skin.

II. Cases with alterations in the blood.

A. Severe anemia with lymphatic pseudoleukemia and aplasia of the bone marrow.

B. Leukemia."

Occasional cases of the complex show a marked *hereditary influence.* Quincke reports the case of a man, aet. 45, with congenital enlargement of both parotids whose father, two uncles, five brothers and two sisters showed the same anomaly.

Tuberculosis, gout and syphilis may be coincident with the complex and influence prognosis materially. Thursfield, whose observations are exceedingly valuable, makes the following statement:

"When there is no involvement of the lymphatic glands or spleen and no alteration in the blood, the disabilities of the affection seem to be confined to the disfigurement, and to a certain degree of discomfort from both of which the lapse of time, one to five years as a rule, releases the patient. When the lymphatic glands or the spleen are enlarged the outlook is more uncertain; of Howard's twenty "pseudoleukemic" cases, six died; and of the definite leukemic cases, Stock's patient alone survived more than six months."

The removal of the enlarged lacrimal glands (Elliott) influenced the salivary enlargements in one case.

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C. Diseases of the Pharynx

(The infectious diseases of the pharynx, including the tonsils, are considered in Section I, Infectious Diseases.)

1. Circulatory Anomalies

(a) *Hyperemia of the Pharynx.*—Congestion of the pharynx may depend upon primary disease, results from local irritation or it may be secondary; it may be either acute or chronic. *Acute hyperemia* accompanies the eruptive diseases of childhood, hence its sudden appearance suggests vigilance and search for infection. In the adult irritating chemicals, highly seasoned or abnormally hot foods, colds, nasal irritation, prolonged or abnormal use of the voice may cause transitory hyperemia.

Chronic hyperemia is due to circulatory, obstructive, chronic local disease or other factors which continually act as irritants. The circulatory disturbances which are paramount are chronic *heart lesions, aneurismal pressure, emphysema* with *heart changes* and *bronchitis, tumors of the neck or mediastinum. Chronic pharyngitis* and *nasal diseases* cause continuous hyperemia. *Tobacco and alcohol* are the most frequent factors in causing chronic pharyngeal hyperemia.

(b) *Hemorrhagic symptoms* may be due to the hemorrhagic diathesis, purpura, local disease, traumatism and occasionally to vicarious menstruation.

(c) *Edema of the pharynx* (uvula and soft palate, peritonsillar tissue) is usually of inflammatory origin with tonsillitis or peritonsillitis, when the prognosis is good. It may be an evidence of stasis (circulatory), pressure, or with nephritis and general edema it may prove threatening.

2. Pharyngitis

(a) *Acute Pharyngitis.*

Acute catarrhal pharyngitis is a common disease, which almost always gets well within a few days. It is an accompaniment of many infections which latter, when it remains limited, are not affected by it. With rhinitis and tonsillitis it is rarely absent. It is often the earliest symp-

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tom of the infectious diseases of early life (exanthemata) though it may be primary and due to any of the causes mentioned in connection with acute hyperemia. The inhalation of all kinds of dust frequently provokes it.

(*b*) *Chronic Pharyngitis*

Preceding acute neglected pharyngitis, tobacco and alcohol, nasal and postnasal diseases, the prolonged use of the voice (clergymen, lecturers, etc.) are the leading causes of chronic pharyngitis. The prognosis is favorable before the changes in the mucosa are not too far advanced for relief of symptoms.

Pharyngitis sicca is never cured until its cause, usually in the nose or postnasal space, has been removed.

(*c*) *Ulcerative Pharyngitis*

(See Syphilis, Tuberculosis, Foot and Mouth Disease and the various infections which it complicates.) The prognosis depends upon the ability to remove its cause.

(*d*) *Phlegmonous Pharyngitis and Retropharyngeal Abscess*

Phlegmonous pharyngitis and retropharyngeal abscess are always secondary, often threaten life by local swelling—edema and associated involvement of the larynx (*edema of the glottis*). *Phlegmonous tonsillitis and peritonsillitis* involve the pharynx and postnasal space. *Sepsis. meningitis, otitis media* and *mastoiditis* are among the dangerous sequelae, also *toxic nephritis.* In rare cases *mediastinitis* and *pneumonia* have ended life.

Phlegmonous pharyngitis with erysipelas or any other infection is never to be lightly regarded. *Retropharyngeal abscess* may follow injury of the mucosa from foreign bodies; its greatest dangers are descending extension, associated *compression, edema* and *pneumonia.* It is always a surgical affection, the favorable outcome depends on the nature of its cause, early recognition and radical treatment. Disease of the cervical vertrebrae, usually tuberculosis, fracture or other bone changes, when associated with retropharyngeal abscess, make the outlook bad.

(*e*) *Ludwig's Angina*
(*Angina Ludovici*)

Ludwig's Angina (first described by Ludwig in 1836) is a phlegmonous inflammation of the connective tissue of the neck, involving, as a rule, the deep and superficial tissue on one side in the submaxillary

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region, though in severe cases it may extend downward and to the opposite side. It is always of infectious origin, is a sequel of streptococcus infection, scarlet fever, infection from contaminated milk (epidemic streptococcus), typhoid and diphtheria. There are cases which are without known primary cause, others which follow injury and infection. The history of these cases prove that with deep constitutional infection, wasting disease and lowered vitality, there may be and often is a prompt sepsis, phlegmonous and gangrenous breakdown of tissue and deep involvement of the sensorium, rapid and feeble pulse, with albuminuria. In such cases the prognosis is grave and life may be in danger for several days. The phlegmonous periparotitis and involvement of the deep fascia of the neck with septic scarlet fever prolongs convalescence and with feeble pulse, nephritis and uremia present a serious complex. Edema of the fauces or glottis or both is always alarming. Idiopathic cases if treated radically early, as a rule, recover slowly after varying periods of sloughing and repair. Ludwig's angina shows marked tendency to *gangrene* within the phlegmonous area. *Sepsis and nephritis* cause the death of a large proportion of such cases. The mortality of the disease is high—the danger period follows several days of slight febrile movement without cerebral symptoms. In unfavorable cases there is a sudden exacerbation of symptoms, collapse, dyspnea, cyanosis, pharyngeal and laryngeal edema, unconsciousness and cardiac insufficiency. Ludwig reported such cases which died before there was time to offer assistance. Dyspnea (asphyxia) is the prominent and threatening symptom. Unless these cases can be reached by surgical means they promptly die. A rally should not deceive the clinician, for relapse and sudden death may follow it. Aspiration bronchopneumonia, pleurisy, edema of the larynx, sepsis, and cardiac toxemia are the leading causes of death.

In pure Ludwig's angina the mouth is always infiltrated and Thomas bases his differential diagnosis on this fact. This is not the case with other forms of cellulitis (scarlet fever) which are considered by many (Osler, etc.) as Ludwig's angina.

Broad of Syracuse has partially reviewed the history and literature of this subject in a paper not yet published and has fully reported a case which terminated favorably. We have taken the following data from Broad's paper:

Davis reported 10 cases with a mortality of 40 per cent.
Sharkey's mortality was 33⅓ per cent.
Thomas reported 106 cases with 43 deaths—40 per cent mortality.

Naturally the percentage of recoveries varies materially if we include the neck infections which are phlegmonous following scarlet fever and other infections, many of which recover. These are not included in the above figures.

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D. Diseases of the Tonsils

(Suppurative Peritonsillitis, Quinsy, Acute Streptococcus Tonsillitis, Vincent's Angina, Chronic Tonsillitis)

(See Section I, Infectious Diseases.)

E. Diseases of the Esophagus

1. Acute Esophagitis

Inflammatory or ulcerative changes of the esophagus are:

(a) Catarrhal (i. Acute or ii. Chronic).
(b) Pustular.
(c) Phlegmonous.
(d) Croupous.
(e) Diphtheritic.
(f) Ulcerative.
(g) Corrosive.
(h) Varices.

The majority of inflammatory or ulcerative changes in the esophageal mucosa are due to thermic insults, chemical irritants, foreign bodies or inflammatory conditions accompanying other diseases.

(*a*) *Catarrhal Esophagitis*

i. *Acute.*—The acute catarrhal inflammation of the esophagus is usually so mild as to give rise to no symptoms. When extensive and deep, as

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it is at times with catarrhal bronchitis, tracheitis, pharyngitis, and acute nasopharyngeal infections and tonsillitis, the membrane is congested, there is epithelial desquamation and some dysphagia. The pathologic process follows the stages of acute catarrhal inflammation and unless there is some serious underlying disturbance it runs its course in a few days and leaves the tube intact.

ii. *Chronic Esophagitis.*—Chronic esophagitis (catarrhal) leads to thickening of the mucosa and submucous tissue with hypertrophy of the muscularis. With alcoholic gastritis it may prove an annoying complication, particularly if limited to the cardiac end when with productive change, stricture may develop. In rare cases *polypi* form.

After acute esophagitis due to corrosive poisons, carbolic and mineral acids, caustic potash, arsenic and other destructive lesions, chronic esophagitis may develop with final narrowing of the tube. The evidences (subjective) may be long postponed in such cases. The obstructive symptoms and physical signs (obstruction to the passing of the sound into the stomach) are often in evidence when the patient presents. Only surgical interference helps these cases. Many are not threatening and live with moderate narrowing of the tube many years. In some cases after caustic poisons have been swallowed, esophageal and aural lesions develop late and are persistent. One of our cases is living over 30 years after swallowing ammonia with deafness and chronic esophagitis.

(*b*) *Pustular Esophagitis*

Pustular esophagitis is secondary to grave infection, as a rule, and is often part of serious constitutional disturbance. *Smallpox* with which pustules form in the esophagus is usually of the malignant type, though not always, and the complication is by no means always fatal. Pustular esophagitis may develop with other infections. The prognosis is not materially influenced by the complication in the majority of cases. It is the primary process upon which the forecast rests. In smallpox the eruption may be present in the mouth, fauces and esophagus at the same time. In most of these ulceration and cure follow.

(*c*) *Phlegmonous Esophagitis*

This may follow from descending extension of phlegmon of the pharynx; it may be associated with poisoning or infection which disrupts the esophagus—usually septic processes. Sepsis and pyemia often cause infiltration, change in the superficial and deep structures of the esophagus. Phlegmonous disease associated with any constitutional infection is always grave, at the same time exceedingly painful.

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(*d*) *Croupous Esophagitis*

Croupous disease of the esophagus may be associated with croupous inflammation in other organs, as croupous pneumonia, croupous laryngitis and rarely there are membranous deposits which are primary—independent entirely so far as we are able to conclude of deposit elsewhere. Croupous esophagitis is usually of streptococcus origin and may be secondary to streptococcus tonsillitis. With most of these conditions the prognosis is good, though as in other forms, most depends upon the nature of the primary infection.

(*e*) *Diphtheritic Esophagitis*

This form of esophagitis is less frequent since the introduction of the antitoxin for diphtheria, though occasionally in neglected or malignant cases, we find the membranous deposit in the esophagus.

The prognosis depends on the nature and extent of the infection as well as on its virulence and the patient's resistance (See Diphtheria, Section I, Infectious Diseases).

(*f*) *Ulcerative Esophagitis*

Ulcerative esophagitis may be cancerous. It may develop in infants while nursing; with long continued disease *decubitus ulceration* may prove painful and serious. *Decubitus ulcers* usually form in the depleted who are emaciated from chronic disease (nervous, tuberculous, chronic and subacute infections of all kinds) and are usually located back of the cricoid cartilage which by pressure against the esophagus causes the "bed sore," for it is that in reality.

Peptic ulcers of the lower end of the esophagus are rare but may form and in the process of healing may cause cicatricial contraction. *Perforation* is exceedingly rare from ulcer, it is a fatal complication (See Rupture of Esophagus). Esophageal ulcers are often *tuberculous* or *syphilitic* (See Tuberculosis and Syphilis).

The prognosis of all ulcerative esophagitis depends on the primary cause—the corrosive ulcer often heals but stricture is to be feared.

(*g*) *Corrosive Esophagitis*

The corrosive may be associated with the phlegmonous form or it may exist alone, it is usually grave. The shock which follows the taking of a corrosive poison is always great. The changes are usually deep and in children and weak adults the prognosis is often bad. Naturally the extent of the corrosion and shock depends upon the kind of poison and dose. In very young children with chronic stricture after swallowing

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corrosive poison the prognosis is unfavorable. We have seen one life saved by the establishing of a gastric fistula in the case of a girl not older than four years with a closed esophagus following the taking of caustic potash. She has lived, so far as we know, now over 20 years, feeding herself through the fistulous opening. If the stricture is fortunately located modern surgery offers some hope.

(*h*) *Varices of the Esophagus*

Varices of the esophagus often form from long continued circulatory obstruction with chronic heart lesions, pressure, Banti's Disease and with liver cirrhosis. Their presence can only be suspected during life when there is rupture and consecutive hemorrhage or when seen through the esophagoscope. The dangers are rupture and depleting hemorrhage. I lost one Banti from erosion of a good sized varix.

2. Spasm and Paralysis of the Esophagus

(*a*) *Spasm of the Esophagus*

(*Esophagismus*)

Esophagismus or spasm of the esophagus is of rare occurrence. It is usually of neurotic—hysterical—origin, alarming to the patient but without danger and, as a rule, of short duration. The patients are usually robust and young. The spasm is sudden in its onset and at once closes the esophagus to solid food, often to liquids as well. In women the associated fear and ungeared nervous condition are, with the spasm, the leading features. Reassurance and suggestion are sufficient in most cases to quiet the patient and overcome the spasm. Any psychic impression in some, as the passing of the stomach tube, particularly in young hysterical subjects, proves sufficient to overcome the symptom. There is, in most cases, recurrence on slight cause and occasionally esophagismus may alternate with spasm of the glottis (laryngismus stridulus), or both may be present together. The element of suggestion proves a powerful factor in the production and the relief of symptoms.

Kindborg mentions incipient cancer as a cause of esophageal spasm. We have never met with a like case.

(*b*) *Paralysis of the Esophagus*

Paralysis of the esophagus is likely to be associated with diphtheritic paralysis in children, occasionally in the adult (see Diphtheritic Paralysis). Its prognosis when not a part of extensive paralysis of other organs, is not bad. *Esophageal paralysis with brain (tumor) and spina*

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lesions, lesions of the spinal bones, remains unchanged, simply one of many symptoms. The same is true of ascending paralysis (Landry's Disease).

3. Stricture of the Esophagus

Stenosis or stricture of the esophagus may be either (*a*) *extra-* or (*b*) *intra-esophageal.*

(*a*) *Extra-esophageal Stricture*

Extra-esophageal stricture is due to compression from without; tumors of the neck, enlarged glands, cystic growths, aneurismal dilatations, mediastinal pressure; tumors (malignant or non-malignant) of the lung and pleura, diseases of the spinal vertebrae associated with tumor formation, abscess, caries or malignant disease of the spine itself, diverticulum of the esophagus, peri- and para-esophageal abscesses, malignant masses springing from the sternum or ribs, pericardial and pleural effusion are among the leading causes which by pressure or torsion narrow the lumen of the tube. Only the removal of the cause, which is almost always impossible, can overcome the stricture.

(*b*) *Intra-esophageal Stenosis*

Over 60 per cent of all strictures of the esophagus are malignant—carcinomatous—and lead to death unless recognized early. Even the early recognition offers practically no hope though surgeons are extending their knowledge and improving their technic and a few are recommending radical interference (See Willy Meyer's Report of Cases, etc.). There are benign growths of the esophagus which cause narrowing of its lumen—these are usually cicatricial following causes which have been mentioned in connection with the various diseases of the esophagus and the productive changes which may follow. Some of these live many years, comparatively comfortable, when constriction is not too great. Most strictures are at or near the cardia, some back of the cricoid cartilage. Stricture of the esophagus when it has existed even a limited time, if very narrow, leads to dilatation above the point of constriction.

The presence or absence of *Meltzer's phenomenon* (Schluck and Spritzgerausch) is of no value in prognosis, though of considerable diagnostic value in individual cases when correctly interpreted. The phenomenon is not present in all cases and according to our experience may in the same case be heard at one time and not at another. The greater the dilatation, as shown by the x-ray or by the amount of fluid or food which it holds, the greater is the obstruction and the more difficult will it be to nourish the patient. We rarely find malignant stricture mul-

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tiple. The dilatation above the stricture is at once associated with narrowing below and collapse of the intestines with, in chronic cases, atrophy of the muscular coat of the stomach and intestines also atrophic changes in the glandular structures. The *cachexia and secondary anemia are in direct proportion to the primary and secondary lesions and the consecutive failure to nourish the patient.*

Symptoms of esophageal stricture after 40, without previous history of esophagitis or ulcer always creates a strong and justified suspicion of cancer. The prognosis of stricture from whatever cause is promptly given, for we have but to consider its pathology. In cases of doubtful origin, non-malignant—the ability to get sufficient food into the stomach either through the esophagus or gastric fistula will soon solve the problem.

Progressive malnutrition, heart weakness and exhaustion is the fate of all of these patients in whom the constriction is extreme.

Congenital stricture leads to death when complete during the early days of life. In other rare strictures though more frequent than the complete occlusion, the lower part of the esophagus opens into the trachea or into a bronchus. We have never met a case in our practice. Thomas (William) has collected 19 cases from medical literature.

4. Cancer of the Esophagus

Neoplasms of the esophagus are, as a rule, cancerous—epithelioma. The lower end of the tube is usually invaded and the growth is annular and constricting. At times the esophagus infiltration is limited and the progress is slow and during a considerable period the stricture may be only partial. We have seen cases in which the growth was so exceedingly slow as to make the diagnosis doubtful. If the cancerous mass is large, the wall of the esophagus and the surrounding structures (glands, etc.) are infiltrated. Metastases may or may not be numerous. Pressure symptoms under such conditions are not relieved and may lead to prompt death. In some cases there is sufficient growth to lead to pressure on the left recurrent laryngeal nerve with paralysis which persists until death. Slight improvement in swallowing may at times prove misleading as may also the vagaries of the disease. With extreme constriction the patient may be able to take solid food during limited periods and be almost completely "closed" in the intervals. *Ulcerative changes* in the growth may make it possible to get more food into the stomach than had previously entered. Alcoholics are subject to cancer of the esophagus; the disease is more frequent in men than women; it is a disease of middle life and is usually primary.

Osler reports 38 cases of cancer in the medical wards of the Johns Hopkins Hospital in 23 years. During the past six years we have seen 8 cases of cancer of the esophagus in 6,300 cases of internal disease.

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We refer the reader to our consideration of cancer as a cause of stricture of the esophagus in this section and repeat what we emphasized, that x-ray examination will lead to localization and will reveal the extent of secondary esophageal changes in most cases. The esophagoscope is a valuable adjunct in the hands of the expert.

Fibrous thickening of the esophagus is secondary to conditions mentioned in this section.

Lipomata and *polypi* are rare—with newer methods these are recognized. We have never met either in our practice.

There can be but one conclusion—the prognosis of esophageal cancer is bad, patients die of starvation usually, though complications, as with cancer elsewhere, may end life. The *average duration* of life in our cases has been between 12 and 18 months after the beginning of subjective symptoms. Unquestionably most cancers of the esophagus are tolerated during long periods before their presence is suspected or cause symptoms.

Metastases may never follow esophageal cancer, on the other hand, a small carcinoma may have multiple metastases—often more than the larger growths. *Metastases* to the mediastinal glands, also enlargement compressing the thoracic duct (Gerhardt) hasten death. Secondary nodules may form in the esophagus itself.

Gerhardt also calls attention to the relative frequency of the association of esophageal cancer and pulmonary tuberculosis.

5. Rupture of the Esophagus

Rupture of the esophagus is exceedingly rare. The wall of the esophagus may rupture as the result of softening (Zenker). Emphysema promptly follows whenever there is esophageal rupture from whatever cause. Traumatism—gunshot wounds, stab wounds, and the ulcerative and infiltrating conditions associated with esophagitis, ulceration and cancer mentioned in this section may occasionally lead to rupture. Death follows rupture promptly in almost all cases from collapse with marked dyspnea, and widespread emphysema. *Perforation or rupture of the esophagus* may cause periesophageal suppuration. *Aspiration pneumonia* may follow fistulous openings into the trachea or into a bronchus. *Perforation into the pleura or pericardium* leads to death from effusion and added pressure. *Pneumothorax* has complicated perforation.

6. Dilatation—Diverticulum

(*a*) *Dilatation*

In connection with esophageal stricture we called attention to the dilatation of the esophagus above the point of closure. This is the in-

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variable result in almost all cases which live any length of time. The extent of the dilatation is a safe guide in deciding upon the degree of narrowing. Röntgen pictures and the stomach tube will prove of material assistance.

(*b*) *Diverticula*

Diverticula of the esophagus may be acquired or congenital. Some forms are multiple, giving rise to small dilatations here and there, causing but few symptoms. Particles of food are likely to fall into the diverticula and cause symptoms. Weakness of the esophageal wall is one cause of dilatation (local) or diverticulum formation. This is the *"pressure diverticulum"* or *"Pulsionsdiverticulum."* The local dilatation increases because of the pressure and retention of food and is most likely to form at the junction of the esophagus and pharynx. *Pulsionsdiverticulum* may dilate to such an extent as to cause pressure symptoms, indeed constrict the esophagus itself when food is held without entering the stomach. The condition is purely surgical. Food is often regurgitated, emptying the sac with temporary relief.

Traction diverticula are not, as a rule, of great clinicial significance. They result either from congenital defects—"embryonal preformed connective tissue strands" which form because of incomplete separation of the trachea and esophagus (Ribbert) or they are secondary to inflammatory changes in the lymphatics, which cause adhesions and consecutive connective tissue contraction which draw upon the esophageal wall causing the localized dilatation. Their presence may not be suspected until a foreign body is caught, ulcerates, causing perforation with consecutive suppuration, mediastinitis and death. Uncomplicated and limited, the presence of the traction diverticulum may never be suspected and is found post mortem.

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F. Diseases of the Stomach

1. Acute Gastritis

Gastritis may be either (1) *acute* or (2) *chronic.* There are several forms of acute gastritis, as follows:

(*a*) *Acute Catarrh of the Stomach*

Acute catarrhal inflammation of the stomach is one of the most frequent of all internal diseases. It is, when uncomplicated, a benign catarrhal inflammation which produces symptoms only of acute indigestion (gastricismus) which yield in the course of two to four days without leaving a remnant. It follows dietetic errors, the taking of excessively hot or cold foods, may result from exposure, sudden atmospheric changes, is an accompaniment of anemia and debility. The *acute alcoholic gastritis* is toxic and is considered elsewhere. The association of *catarrhal gastritis with duodenitis* may cause jaundice (See Catarrhal Jaundice) and postpone recovery. The *stomach contents* in most cases of catarrhal gastritis offers nothing of value. In aggravated cases the free hydrochloric acid may be reduced, the digestion is tardy; there may be acetic and butyric acid, a few blood corpuscles and increased mucus.

(*b*) *Infectious Gastritis*

The infectious type of gastritis follows the ingestion of contaminated food or may be due to an endemic in which many are attacked at the same time (probably streptococcus). Catarrhal grip may also be present at such times. During epidemics of true grip the *influenzal type of gastritis* or infectious gastritis is frequently met. Such cases include symptoms which make the patient uncomfortable (localized pain, localized tenderness, vomiting, nausea, hypersecretion, "bilious" vomitus, with the usual malaise and weakness of influenza).

Infectious catarrhal conditions of the nasal and upper respiratory passages as well as the pneumonias may be associated with gastritis. With all of these conditions the localized stomach infection is not usually of paramount importance but the primary disease and the patient's resistance are most important in offering a forecast. In old people and in the weak the added infection of the stomach may help to undermine resistance but such influence is exceedingly rare as the stomach changes are few and superficial.

(*c*) *Phlegmonous Gastritis*

Phlegmonous gastritis is exceedingly rare. Associated with the grave infections as typhoid fever, smallpox, pyemia, sepsis and abscess, it com-

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plicates already existing serious disease, and adds to the dangers. With puerperal fever and with caustic poisons or erysipelas, the complication is extremely grave.

(*d*) *Membranous Gastritis*

Membranous gastritis is almost always of diphtheritic origin, therefore, secondary and is exceedingly rare. There may be no subjective symptoms of stomach invasion or there is pain, tenderness, vomiting, tense abdomen, particularly in the epigastrium. The heart is rapid and offers the leading prognostic data. The temperature cannot be relied upon because it may not be materially influenced by the complication. The malignancy of the primary infection and general condition of the patient, including the heart, make prognosis certain. In the favorable cases convalescence begins with the third week.

(*e*) *Toxic Gastritis—Corrosive Gastritis*

Acute alcoholic gastritis is one of the most frequent of all the diseases of the stomach mucosa. It is simply one of several changes wrought by the poison and with proper care promptly yields to treatment. Most alcoholic toxic gastritis is superficial and catarrhal, is associated with great nervousness—unrest and insomnia—at times albuminuria—but all of these symptoms, unless there are marked depression, heart and other nervous symptoms and lesions, yield. The persistent use of alcohol leads to chronic changes (chronic gastritis). Other poisons which cause gastritis include the mineral acids, alkalis, lead, mercury, phosphorus and arsenic frequently.

The *caustic and corrosive effect* of these poisons with the associated shock and kidney involvement often promptly lead to death. In these cases there are deep changes in the mucosa and prompt degeneration of the heart.

The decomposition of albuminous substances, either directly or through the circulation, may cause threatening symptoms of toxic gastritis. Alt has attributed gastritis to the excretion of toxalbumins by the stomach in cholera and Lauder Brunton and Fayrer suggested its production by the excretion of the cobra venom. Alt confirmed their suspicion. The vomiting in many general infections may be traced to primary toxemia and secondary gastritis (Brunton).

(*f*) *Acute Gastritis with Organic Diseases of the Stomach*

The presence of acute gastritis with organic diseases of the stomach during exacerbation is among the possibilities and may account for some of the symptoms which are evanescent. The permanent symptoms are often an expression of final chronic changes in the mucosa.

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(*g*) *Acute Gastritis of Fungus Origin*

Acute gastritis of fungus origin (yeast, anthrax, favus and the Oidium albicans) is only persistent when neglected. The same may be said of gastritis due to the presence of animal parasites.

(*h*) *Acute Suppurative Gastritis*

There are rare cases of acute suppurative gastritis in which there is perigastritis with abscess formation in the wall of the stomach. The evidences of profound pyemia—sepsis—are prominent and death is the rule. With the suppurative there may also be phlegmonous gastritis.

Children often suffer from recurring acute gastritis with fever which continues only during a few hours or from one to two days. These attacks are due to faulty diet or other trivial causes in those who are said to have "weak stomachs" or "poor digestion." With the advent of the 6th or 8th year the intervals between the attacks grow longer and cease entirely usually after the tenth year. There are adults who are subject to the same acute exacerbations of short duration at long intervals. Cautious differentiation is necessary as some of these are due to chronic appendicitis, gallstones, are of central or spinal origin (cerebral syphilis, tabes dorsalis, etc.).

The diagnosis of acute gastritis is not always easy, and prognosis therefore becomes fallacious. The experiences of the past two decades prove the frequent presence of stomach symptoms "gastritis"—"acute dyspepsia" in a surprisingly large number of abdominal and other conditions, in which the stomach is absolutely normal.

2. Chronic Gastritis

(*Chronic Catarrh of the Stomach, Chronic Dyspepsia*)

Chronic catarrh of the stomach is an inflammation of the mucosa characterized by marked increase of mucus, changes in the gastric juice and in the advanced cases hypertrophy of the muscular coat; increasing thickening and proliferative change in the mucosa, atrophy of the gastric follicles and decided proliferation of the submucous tissue. Polypoid and cystic growth may develop. In some cases there is no hypertrophy of the muscularis but a weakening and dilatation of the wall. In a minority of cases the productive change leads to *cirrhosis of the stomach.*

Cirrhotic Gastritis

(*Brinton's Disease, Linitis cirrhotica*)

In this form of the disease the interstitial overgrowth predominates, the stomach is abnormally small and there are atrophic changes in the infiltrated mucosa upon which in individual cases multiple polypi may rest.

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Productive change in cases of stomach cirrhosis may cause pyloric obstruction and simulate carcinoma; the cirrhotic stomach may also simulate infiltrating cancer.

The *forms of chronic gastritis* which we consider are either *parenchymatous, interstitial* or there may be *mixed types* in which lesions are irregularly disseminated and are both parenchymatous and interstitial. There are but few cases of long continued gastritis in which the interstitial changes do not largely predominate and with the advance of the process there is loss of tone, motor insufficiency with final dilatation. We have seen cases in which after years of insult to the stomach the atrophy has been so extensive as to leave but little remnant of the original mucous membrane (anadenia gastrica). Gastritis may be (a) *primary* or (b) *secondary.*

(a) *Primary gastritis is usually attributable to the patient's own fault; alcohol, excessive drinking and eating are the leading etiologic factors.* Poisons and irritants, improperly prepared food, faulty preparation of the food in the mouth for the stomach (faulty mastication, fast eating) irregularity in eating are also sufficient to start and continue primary gastritis.

(b) *Secondary gastritis* depends upon other and primary organic disease of the stomach, cancer, pyloric obstruction and dilatation, long continued atony of the stomach wall and circulatory faults causing chronic enlargement of the mucosa from valvular diseases of the heart, pulmonary diseases (emphysema, chronic pneumonoconiosis, asthma, malignant growth or pressure, etc.). Kidney lesions with chronic uremia (chronic nephritis, etc.), obstruction within the portal circuit, syphilis, pernicious anemia and many other grave primary diseases. In the secondary gastritides the added stomach invasion is weakening, often an important factor, though the primary disease usually causes general stasis hence prognosis becomes a complex problem but always rests on the paramount influence of the initial and responsible lesion. Often secondary gastritis depending on primary incurable disease may improve materially; there may with heart lesions be long periods without symptoms. The gastric features vary as do physical signs and symptoms when the primary condition is influenced by rest and treatment. Cases in which *chronic gastritis* is associated with or secondary to *cirrhosis of the liver* may be far advanced in organic change and yet with latency of the latter disease and proper care, life may be made comfortable and indefinitely prolonged. We often find post mortem evidences of both conditions in subjects who had, during many years discontinued alcohol.

In *chronic gastritis* there is usually subacidity though there are cases with normal acidity and as Boas has demonstrated there is a characteristic type in which there is hyperacidity (*gastritis acida* or *hyperpeptica*) or hyperacidity may be present temporarily.

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The symptoms which predominate comprise the complex of *chronic dyspepsia. I do not consider chronic dyspepsia a disease per se but always a complex of either primary or secondary gastritis or an accompaniment of other disease with complicating gastritis or faulty gastric function.* (The Nervous Dyspepsia of Leube.) The symptoms of chronic catarrhal gastritis, including the excessive production and morning vomiting of mucus, anorexia, pyrosis, epigastric pressure, at times pain, persistent nausea, with irregular bowels, coated tongue, all aggravated and continued by the patient's indiscretions (alcohol, faulty eating, etc.) even in advanced cases, may yield to rational treatment and temperance. It is surprising to note how promptly these symptoms yield. The change does not indicate a return of the gastric mucosa to normal but the *insult* discontinued, the remnant of tissue with the assistance of the intestinal digestion proves sufficient. The mucus secretion in such cases, particularly the alocholic, will be fairly well controlled. Such cases are always ready to relapse on slight provocation particularly on the return of the original cause.

The nervous manifestations in the above mentioned cases are usually as readily controlled as are the other symptoms.

Stomach Contents

The examination of the stomach contents in chronic gastritis is of considerable value in deciding upon the type of gastritis present, but for prognosis it offers but few data save in those forms in which it establishes the advanced atrophy of the gastric follicles and complete *anadenia gastrica* or *achylia gastrica* with or without primary constitutional disease (pernicious anemia, diabetes mellitus). In all of these cases the microscopic examination is important. The presence of nuclei in the epithelial cells is suggestive of acid gastritis (Stockton). The presence of large quantities of mucus in the vomitus or expressed content is not *per se* unfavorable for the relief of symptoms. The majority of such cases are dependent upon removable causes (alcohol, etc.).

Hyperacidity with *gastritis acida* is at times rebellious to treatment and when relieved tends to recur on cause but in the end it is controlled but only with the assistance of the patient.

During the early stage of alcoholic gastritis hyperacidity is frequent. Unless conditions are improved there is progression with gradual reduction of free hydrochloric acid and other evidences of disturbed function, particularly motor insufficiency. *The presence of free HCl in the empty stomach* in these cases often persists during long periods until with the advancing atrophy the acidity falls and there is increase of *organic acids* (lactic, butyric and acetic).

Anadenia or Achylia Gastrica.—The anadenia gastrica of Ewald or achylia gastrica offers evidences of far reaching atrophy with, in most cases, normal motor function. *Anacidity* in chronic gastritis does not

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always indicate atrophy of the mucosa for it may be due to gastric neuroses.

Pepsin and rennin are usually present and vary with the free HCl.

Single examinations of the stomach contents are not always dependable. The secretion often varies from day to day and faulty conclusions are reached unless repeated examinations are made. In many, psychic factors are potent in influencing stomach function. There is usually a large *psychic element* which demands consideration in connection with the examination of the stomach contents in the alcoholic as well as in some cases of gastritis which are of secondary origin.

Chronic Gastritis.—The extreme nervous state of the alcoholic with acute exacerbations of chronic gastritis is often controlled with great difficulty. Such patients are usually steady drinkers and not a few develop wet brain (Alcoholic Meningitis). With the nervous symptoms there may be "stomachal vertigo," a condition which Trousseau described, patients fear the "sinking into an abyss"; *vertigo* may be of the *labyrinthine type; melancholia, hypochondriasis, changed disposition, erratic heart, polypnea, morning cough, hiccough, dysphagia* and *asthma with cyanosis* may all yield with the improvement following proper diet and abstinence in primary cases and improvement of underlying conditions in secondary gastritis.

Remissions and exacerbations are to be expected in all forms of primary gastritis depending largely on the habits of the patient. Many alcoholics live for years without subjective symptoms, who finally develop them. Such cases are controlled with great difficulty. The *blood picture* in those forms of anadenia or complete atrophy may resemble pernicious anemia or with cirrhosis of the stomach and thickening of its coats, with palpable small stomach there may be a strong suspicion of carcinoma. Such cases may, with proper treatment, improve materially for as with all gastritides, however far advanced, the digestive function of the intestinal tract may prove sufficient to supplement the gastric. It will be noted in all organic diseases of the stomach that symptoms are long tolerated without revolt, that digestion proves sufficient to carry the patient along without loss of flesh or many subjective symptoms during long periods while the organic changes are advancing insidiously.

The *changed and degenerated or infiltrated mucosa* in chronic gastritis never becomes normal. It may be so little changed as to cause no serious disturbances. Symptoms may disappear during interminable periods, periods of remission may be short, permanent cure, i. e., regeneration of peptic glands, removal of new connective tissue is not to be expected. Once the subjective symptoms are present they may, in spite of improvement or remission be expected to recur on slight cause.

Alcoholic Gastritis.—Alcoholic gastritis which has existed during long periods may, after only short abstinence, show marked improvement and

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with continued abstinence may never again give rise to symptoms. The improvement following treatment is promptly manifest in many cases. With motor and absorptive faults and *pyloric obstruction from interstitial thickening* the dilatation which follows is likely to remain; the general condition depends upon the ability of the intestines to supplement the work of the stomach and the direct result of the gastrectasia. The *duration* of uncomplicated primary gastritis in which the atrophy of the follicles is not too far advanced, and does not progress may be many years. Gastritis without other organic diseases without advanced atrophy, detected early and properly treated, may never give rise to symptoms, in spite of the changed mucosa.

The *complications of primary gastritis* are few and of no prognostic import. The many primary conditions which lead to secondary gastritis are each likely to be associated with conditions which must naturally influence prognosis independent of the existing gastritis. *Severe secondary gastritis,* uncontrollable vomiting, and toxic symptoms sometimes threaten cases in which resistance has been reduced. We have never known death to be due to chronic gastritis alone though the general condition is often below par and efficiency is reduced.

I know of no other chronic disease in which rational treatment and the coöperation of the patient in primary cases so promptly and thoroughly control symptoms. *Symptoms of "chronic dyspepsia" without stomach lesions* may remain uncontrolled and lead to faulty diagnosis in a large number of cases unless great caution is used. Most of these are due to *chronic appendicitis, gall-stones, cirrhosis of the liver,* or *spinal lesions,* mainly *tabes dorsalis.*

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3. Dilatation of the Stomach—Gastrectasia

According to Ewald the stomach which continually holds more than 1,600 c.c. of fluid is abnormally dilated. Such stomachs are found to hold food longer than seven hours.

Dilatation of the stomach may be either (a) *acute* or (b) *chronic.*

(a) *Acute Dilatation of the Stomach*

My experience with acute distention of the stomach beyond its normal capacity has been limited to its occurrence with chronic disease, acute

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infections and following anesthesia, usually for abdominal conditions. The *gastrectasia* in all of these cases has been sudden in its onset, has at once been associated with symptoms of failing heart and collapse, vomiting of large quantities of fluid, pinched features and—unless the condition was at once correctly interpreted and treated—death followed.

I have found *acute dilatation of the stomach an occasional serious complication of pneumonia.* If it arises suddenly during the height of the disease it may promptly lead to death.

Sudden gastrectasia with pneumonia and chronic valvular disease is usually fatal. Fussell has recently reported his experiences with this dangerous complication. In all of Fussell's cases the autopsy showed constriction of the duodenum at the root of the mesentery.

There is in all probability involvement of the innervation leading to dilatation, this in itself causing by traction a constriction of the duodenum. Fagge's original description of these cases was based upon his observations in a case in which the patient had overeaten, and with classic symptoms died in collapse. Connor of Cincinnati reported 102 cases of which 42 followed anesthesia. In the midst of typhoid fever, as in pneumonia or with chronic heart lesions, without added infection, blows upon the abdomen or from any other cause unless the symptoms are promptly relieved by lavage of the stomach and stimulation, recovery is exceedingly rare. It is possible for patients convalescing from acute infections to suddenly fall into collapse from dilatation of the stomach, when with peristaltic unrest, marked splashing and collapse with all of the usual physical signs, their lives are threatened. Relief must be prompt, for unrelieved, death follows in a few hours. We have had no experience with suddenly arising dilatation in spinal disease. Connor's cases showed the usual high mortality, practically 75 per cent. The prognosis is favorably influenced by the early lavage and turning the patient on the side to encourage the emptying of the stomach. The latter maneuver alone (without lavage) is of little value. Of 31 patients treated with medicine alone without posture or tube, 29 died; in 142 cases after operation the mortality was 54.9 per cent according to Borchgrevink, who found that in 70 cases treated with the tube and following Moynihan's advice to turn the patient on the right side, the mortality was 26.9 per cent. Meltzer suggests that the dyspnea with frequent swallowing of air without saliva may be a factor in the production of the dilatation.

(*b*) *Chronic Dilatation*

Chronic dilatation of the stomach is *rarely primary;* when it is, it may be characterized as *myasthenic* or *atonic,* and according to Boas represents *"motor insufficiency of the first degree."* Primary myasthenic dilatation is usually due to the patient's own fault—errors of diet, fast and in-

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ordinate eating, the excessive drinking of fluids (alcohol, beer, tea, coffee and water). There are primary myasthenic dilatations which are *congenital;* families are found in whom all members are afflicted. Dilatation which is chronic and due to myasthenia or atony, may be materially improved by treatment, but it is likely to recur and often leads to continuous ill health and persistent dyspepsia. When due to nervous *influences* which can be controlled unless the stomach wall is abnormally thin and the condition of long duration, the prognosis is good for the relief of symptoms but more or less dilatation usually remains. Enormous and unexplained gastrectasia is often found in the insane, with wasting diseases, diabetes, and in tabetics.

Atonic dilatation which can only be explained on the theory of myasthenia without organic change, is often associated with nervous symptoms which are persistent and exceedingly annoying. They often include the complex of neurasthenia and in women, oftener than in men, continue uninfluenced by any treatment. In both there is a large element of suggestion which continues and is responsible for many of the subjective features.

Stomachal vertigo (Trousseau-Friedenwald) is exceedingly annoying in this form of dilatation as it is in chronic gastritis. It is unquestionably of toxic origin. Boerhave recognized it; Trousseau first described its leading features; Boas, Friedenwald and Pick have all insisted on its toxic origin.

The observers mentioned in the preceding paragraph found atony of the stomach and intestine the leading cause of stomachal vertigo. Enormously large stomachs—*gastromegaly*—may continue unchanged throughout life, without causing symptoms. The motor and digestive functions remain undisturbed.

Secondary Chronic Dilatation

Dilatation of the stomach which is secondary and chronic is dependent upon *obstruction.* The obstruction is either *benign* or *malignant.* There are a number of extragastric lesions which by compression or traction lead to secondary dilatation of the stomach. Whenever from any cause there is constriction of the pylorus, the stomach wall makes an extra effort to empty the organ and hypertrophy of the muscularis results, and with moderate non-malignant disease, may, during unlimited periods prove sufficient, giving rise to no or few symptoms. When the stomach is forced to overcome increasing obstruction, its musculature suffers; degenerative changes may follow in its wall; there is increasing consecutive dilatation. The degree and amount of secondary change depend entirely upon the extent and nature of the obstruction. If the obstruction cannot be overcome by mechanical or surgical means, complete insufficiency follows, and the stomach is continuously distended with undigested and irritating solid

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and liquid food. With these cases the *toxic and nervous symptoms* are in the ascendency and long periods of ill health and the neurasthenic complex are thereby explained, though not always relieved.

In all of these cases lavage is likely to relieve the subjective complaints; unless the primary cause can be removed or overcome, subjective and objective manifestations can only be treated symptomatically. These cases when neglected may develop *tetany* which is always threatening, demanding immediate care. Lavage may prevent the spasms during unlimited periods (See Tetany). There are chronic cases in which changes of a degenerative character or inflammation secondary to serious constitutional anomalies lead to muscular insufficiencies and consecutive dilatation. Such cases are not materially influenced by treatment.

The organic constriction at the pylorus, either intra- or extragastric, produces *motor insufficiency of the second degree* and provokes persistent symptoms of dyspepsia.

The prognosis of secondary dilatation of the stomach can only be offered with the separate consideration of the responsible lesions. The chapters which follow (Benign and Malignant Stenosis of the Pylorus, Ulcer of the Stomach, etc.) offer the necessary data which justify the forecast.

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4. Gastroptosis—Enteroptosis

(*Glenard's Disease, Visceroptosis*)

Glenard's disease is a condition in which there is ptosis of the abdominal viscera, *gastrectasia, gastroptosis, enteroptosis,* often *prolapse of the liver and spleen,* with—in a large number of cases—*mobile kidney.* There is, in most cases a train of prominent nervous manifestations, often but few gastro-intestinal symptoms. The neurasthenic complex is always in the ascendency and is the leading feature, besides the physical signs of the disease. While incorrect dress (lacing, etc.) may increase prolapse in individual cases, there is, as a rule, a *predisposition to Glenard's disease* and this is greatest in the children of neurotic parents, themselves

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nervously overwrought. Any anomaly which removes the normal support of the abdominal organs—child-bearing, laceration of the perineum, injury to the abdominal wall, ventral hernia following laparotomy, abnormal "ligamentous and cartilaginous support" (Stockton)—may lead to prolapse of the abdominal viscera. The congenital loose attachments of the mesenteric and peritoneal supports are leading features.

Stiller has demonstrated the absence of the tenth costal cartilage in a large number of cases of Glenard's disease. We have been surprised by the frequency of this anomaly, the marked and persistent neurasthenia in such cases. The absence of the normal dorsolumbar curve is considered by R. R. Smith as a leading feature of enteroptosis, and both Smith and Goldthwait agree that the condition is of hereditary origin. Great caution in diagnosis is necessary, for Röntgen pictures have proved the fact that most adults have more or less enteroptosis and we are of the opinion that too many x-ray pictures are faultily interpreted to the injury of the patient (Holzknecht-Groedel). We are fully agreed with Stockton who in his recently published works says " . . . insufficient value is attributed to the effect of gravity in dragging down viscera weighted with bismuth."

We are fully convinced that cautious physical examination of the abdominal viscera offers the most valuable data for diagnosis and prognosis which should in doubtful cases be confirmed by the Röntgen rays, but the latter need interpretation by the specialist who is not biased by preconceived notions or uncertain theories. We have, in lean subjects, frequently obtained valuable data from inflation of the stomach and rectum with carbonic acid gas or air. *Auscultatory percussion* is also of great value.

Splashing is a symptom of value only as it is considered with other physical methods and x-ray in doubtful cases. The most difficult cases are those in which without cause, save inherent defects, we find the fully developed *Glenard's process with overpowering neurasthenia,* at times psychoses, which are borderline; in all an overpowering autosuggestion which holds the patient without thought of anything but self. Often there are *imperative conceptions* which make life almost unbearable. *Mobile kidney* is as a rule a permanent defect and in most cases causes no symptoms; its presence when disregarded or unrecognized by the patient will be well borne during years, often forever.

Treves, with others, has found that the larger number of "anchored" kidneys finally loosen from their moorings and are, after a few years, as movable as before. There are exceptions but they are few, and the consensus of opinion today favors support without operation.

Dietl's crises are exceedingly painful and when frequent may interfere with the general health of the patient besides leading to morphinism. These cases are favorably influenced by mechanical treatment or radical surgical operation.

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The twisting of the ureter may cause repeated *intermittent hydronephrosis*, not a serious complication, for with positive diagnosis and surgical treatment, after scientific differentiation (cystoscopy, ureteroscopy) the condition may be overcome. The functional tests should include the consideration of both kidneys. The *circulation* is often erratic and functional disturbances are not unusual; there may be palpitation and arhythmia with, in some cases venous engorgement. Many of these symptoms are promptly relieved by support or postural treatment. They return on slight cause.

Chronic constipation is the bane of these cases and cathartics are taken by the majority. Support, diet and rational treatment improve many of these.

The prognosis so far as life is concerned is always good; the neurasthenic symptoms in uncontrolled cases (usually in women, though men are frequently included) are likely to persist unchanged until after the years of greatest sexual activity, after which we have found enormous improvement. The element of suggestion with proper support, right living and occupation, are the paramount factors which influence the lives of these patients (See Neurasthenia).

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5. Pyloric Obstruction

Stenosis of the Pylorus.—Pyloric obstruction, or stenosis, may be either *benign* or *malignant.* The malignant stenoses of the pylorus are considered with cancer of the stomach.

Benign Stenosis of the Pylorus

Benign stenosis of the pylorus may be either (a) *functional* or (b) *organic.* The latter may be (I) *congenital* or (II) *acquired.*

(a) Functional Stenosis

Functional stenoses are found in the highly neurotic, and are transitory. *Pyloric spasm* may be chronic and lead to gastrectasia with intol-

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erant stomach, peristaltic unrest and hyperacidity. These patients are made worse by mental distress; they are often neurasthenic. While the spasm does not continue indefinitely, the gastrectasia may persist and the spasm is likely to recur on slight cause.

Intermittent hyperchlorhydria without ulcer may cause pyloric spasm and temporary obstruction; in such cases the pains (always present), large fluid hyperacid vomitus, severe headache and other cerebral symptoms, yield to proper treatment. The symptoms persist until the hyperacidity is overcome.

Acute dilatation depending on transitory causes (obstruction due to traction) has been separately considered (See Gastrectasia).

Pyloric spasm may be safely considered secondary in most cases, and its presence should lead to a strong suspicion of organic disease. In young neurotic girls pyloric spasm may be associated with moderate gastrectasia, and there may be peristaltic unrest, painful cramping of the stomach, with or without vomiting. With increasing methods of precision, functional stenosis of the pylorus will be found less frequent.

(b) Organic Stenosis

(1) *Congenital Stenosis of the Pylorus*

If congenital stenosis is of moderate degree, manhood may be reached in comparatively good health; nature may compensate for the defect, the stomach musculature increasing and digestion continuing practically normal (*compensatory hypertrophy*).

Serious congenital stenosis proves its presence in symptoms before the fourteenth day—never after the ninth week—and death follows before the fourth month unless the infants are relieved by surgical interference. Cases which appear extreme may (rarely) yield unexpectedly. One of our cases, with symptoms beginning at birth, in which the child during the first two years of life presented all of the symptoms of congenital stenosis (before the days of the x-ray), has grown to manhood, perfectly well. When this boy was one year old he weighed less than he did at birth.

Persistent vomiting in children beginning after the ninth or tenth week of life, is not due to congenital narrowing of the pylorus, and offers a better prognosis than does the vomiting of stenotic origin.

Most children with congenital stenosis die before the end of the third or fourth month.

No possible modification of the food relieves the symptoms when the stenosis is of high degree. Congenital incomplete stenosis of the pylorus causes chronic disturbances which continue throughout life.

Stagnant food is always present in the stomachs of these patients. Dilated stomach persists in spite of well regulated treatment, lavage, etc.

Gastric fibrosis of Hanot or the *hypertrophic pylorus of Cruveilhier*

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and Andral are sequelae which materially influence the size and position of the organ.

(II) *Acquired Stenosis—Intrapyloric*

1. **Chronic Cicatricial Stenosis.**—The majority of benign stenoses are due to ulcerative processes invading the pylorus. Ulcers may exist without causing symptoms; usually the history is direct and convincing. Cicatricial contraction follows slowly; in many there is the history of hemorrhage. The stomach contents, the x-ray and the tube confirm the dilatation and primary lesion.

Phlegmonous sloughing due to corrosive poisoning and contraction cause dilatation. The prognosis in otherwise normal adults is excellent following surgical interference.

2. **Fibrotic Stenosis.**—(a) *General Stenosis.*—General stenosis was described by Brinton and Hanot (See also *Brinton's Disease or linitis plastica or cirrhosa*). The change is far-reaching in the mucous and submucous coats of the stomach, invading the pylorus as the process advances, leading to marked contraction and thickening of the entire organ with almost complete closure of the stomach outlet. Pernicious anemia may be simulated—also cancer. Surgery offers the only hope of relief in extreme cases.

(b) *Localized Stenosis.* Localized fibrous thickening of the pylorus is likely to be annular. Previous limited ulceration may be the cause. Ring-shaped constriction causes consecutive dilatation. These cases are also favorably influenced by radical treatment.

3. **Hypertrophic Stenosis of Cruveilhier.**—Hypertrophic stenosis of Cruveilhier fully described by Boas, follows chronic gastritis; there is ultimate dilatation. The prognosis depends upon the general condition of the patient and the ability, if the symptoms are threatening, to withstand surgical interference. Most cases are not so extreme that they demand radical treatment and may live for years without it.

4. **Stenosis Dependent upon Active Ulcer.**—Ulcer at or near the pylorus and in the first part of the duodenum with associated spasm, marked swelling which may be acute or due to secondary inflammation, is an occasional cause of pyloric constriction and offers a good prognosis.

5. **Acute Inflammatory Stenosis.**—Acute inflammatory stenosis associated with infection, deep seated gastritis and acute poisoning may subside unless the changes are sufficiently deep to give rise to permanent lesions (Elsner).

6. **Syphilitic Stenosis.**—Syphilitic stenosis is occasionally found; when extreme and the treatment radical, improvement may follow. Syphilis is a frequent cause of stomach symptoms which are transitory, disappearing on treatment, but if secondary dilatation follows it remains but little influenced.

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7. **Tuberculous Stenosis.**—Tuberculous stenosis is rare and is not limited. The process is far-reaching and involves the entire stomach.

8. **Stenosis dependent upon non-malignant growths,** fibromyoma, adenoma and polypi may prove puzzling; they are rare and are diagnosticated either during surgical interference or post mortem.

9. **Stenosis due to distortion or traction causing acute pyloric obstruction** (Kussmaul, Aufrecht and Riegel), dragging at a point in the horizontal part of the duodenum, is practically identical with acute dilatation already considered. These cases are always serious (mortality 75 per cent). (See Acute Dilatation of Stomach.)

Extrapyloric Stenosis

"It is difficult to divine all of the unusual and unexpected conditions which may lead to extrapyloric organic stenosis" (Elsner). The leading extrapyloric lesions which constrict the pylorus are: perigastritis, gall-stones, adhesions to neighboring organs—particularly to the liver and gall-bladder—distortions due to innumerable anomalies and pathologic changes invading the organs already mentioned, also the pancreas and kidney. The pylorus is constricted, and motor insufficiency with dilatation results.

We have reported monstrous gall-stones which by pressure and adhesions caused stricture with symptoms of cancer (Elsner). It is at times exceedingly difficult to recognize the cause of extrapyloric stenosis; in the majority of cases diagnosis and prognosis are possible and with modern surgical technique the cause is often removed. Each case demands separate consideration that the underlying cause may be discovered and considered.

In the prognosis of pyloric stenosis we must cautiously differentiate benign and malignant disease. The diagnosis of constriction must always be suspected when the fasting stomach is distended and contains food. *Food remnants after seven hours prove motor insufficiency and suggest obstruction. The obstruction creates a decided disproportion between the stomach's task and its ability to perform its duty* (Riegel).

Dangers from tetany are separately considered (See Tetany).

With advancing disease the *heart* may become ungeared; it influences the length of life in cases which are not amenable to surgical treatment. The stomach content which shows gradual loss of HCl from time to time with the addition of organic acids as the free HCl disappears, evidences of fermentation must lead to a strong suspicion of malignancy and argues against benign disease. Large quantities of *indican* in the urine and an *abnormally high urea output* are suggestive of malignancy, and argue against benign constriction.

X-ray examination proves exceedingly valuable, for it localizes lesions, outlines the stomach, and with the results of thorough physical examination

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and the chemical analysis of the stomach contents makes a forecast reasonably certain.

With incomplete obstruction, persistence, prophylactic treatment and diet, will often hold the disease without advance. Diet requires special care, because of the weakened motor function and obstruction, that food may be forwarded beyond the point of resistance for further digestion. If this can be accomplished, life may be prolonged many years in the absence of complications.

The prognosis is improved in proportion to the ability of the attendant to prevent stagnation and the formation of organic acids. This means that the distended stomach must be assisted, so far as it is possible, to empty itself. In no other disease of the stomach will detail and clear judgment with the full appreciation of the primary cause of the stenosis accomplish so much.

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6. Gastric and Duodenal Ulcer

(Ulcer of the Stomach, Peptic Ulcer, Round Ulcer of the Stomach)

Symptoms.—Round ulcer of the stomach is characterized by circumscribed loss of the mucosa, which when it becomes chronic shows but slight tendency to heat.

History.—Our first conception of the disease dates from 1829 when Cruveilhier fully described it. The early literature is most interesting and proves how full was the knowledge which the clinicians possessed before our modern refinements of diagnosis were introduced. Following Cruveilhier, Rokitansky, the great pathologist at Vienna (1804-1874), wrote a classic treatise on *ulcus ventriculi.* Virchow in 1853 advanced the theory that the break in continuity of the mucosa depended upon a quantita-

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tive anomaly in the elaboration of free hydrochloric acid caused by vagus disturbance and that the circumscribed ulcer (limited) was associated with a local anomaly with the choking of the circulation.

In 1858 Brinton's work appeared; Trousseau in 1860 followed and prepared the foundation for rational medical treatment; the same year L. Miller, a practicing physician in Minden, published as Leube says, the best treatise which we possess on the disease; 1864 brought Bamberger's work, 1878 Lebert's. Later Leube proved the overpowering influence of rest, diet, and rational treatment in the majority of cases, since which time the works of Riegel, Ewald, Boas, in Germany, in the domain of medicine, the Mayos, Rodman, Musser, Stockton, Jacobi in America, Robson and Moynihan in England, stand out in bold relief among the thousands of contributions dealing with the surgical and medical problems, many of which are still unsettled. All of this activity has led to many positive conclusions—better than all else, to the saving of human life because of our appreciation of the dangers of complications and sequelae, and their conservative, often radical attack.

General Considerations.—The forecast of stomach ulcer depends upon its type and depth, the local secondary changes, the resistance, the blood state, the complications, and the time when treatment (dietetic, medical or surgical) is instituted.

Aschoff's hemorrhagic erosions cause small multiform tissue loss; the erosions are round and sharply defined, usually located in the fundus; there are but few or no lesions at the pylorus. These hemorrhagic ulcers were supposed to be of embolic origin, but in the light of recent experiences this theory has been questioned. Septic and fat emboli may certainly cause hemorrhagic infarct, and venous emboli (Aschoff) have been considered. Hemorrhagic erosions are rarely found in adults, almost always in infants. When found in the adult they follow abdominal operations; they may cause subjective symptoms during a short time preceding death. Their formation is usually a terminal feature. The loss of blood connected with hemorrhagic ulceration is not large and is not a factor in prognosis. The infection or toxemia in these cases remains the prominent feature.

Large hemorrhage into the mucosa may in the adult lead to acute multiple ulcers in the fundus and at the pylorus. The posterior wall is their favorite seat. *Fatal hemorrhage* even from small ulcers is possible; the stomach is filled with blood and the ulceration is found to be deep, not simple as in the cases considered in the previous paragraph. These cases are in all likelihood *mycotic;* they may follow *traumatism, thrombosis* (secondary to coronary thrombosis, to gall-bladder infection, thrombosis of the cystic vessels or embolic closure of the artery). With *arteriosclerosis* and *nephritis, acute ulcer of the stomach* has formed (Hauser, Ophuls). *Whatever the method of formation, the majority of acute ulcers heal leaving sufficient evidences to prove that possibility* in the light colored cica-

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trix, usually superficial, which rarely causes secondary motor insufficiency or stenosis. *In a proportion of cases the chronic round ulcer results from the acute.*

Aschoff makes the positive statement that "the chronic ulcer almost always originates after an acute defect." The question, therefore, is not how does a chronic ulcer originate but under what conditions is the "acute defect" transformed to produce it.

Between 85 and 90 per cent of chronic ulcers are found at or near the pylorus. The duodenal ulcers are near the pylorus in the first and second portion of the duodenum. Twenty per cent of Mayo's cases involved the margin of the pyloric ring.

The thorough observations and recorded experiences of surgeons during the past decade, particularly those of the Mayos, Moynihan, Deaver, Robson and others, who have had control of an enormous material which has been scientifically examined and treated, have revolutionized our ideas concerning many points bearing on diagnosis, prognosis, and rational treatment of all necrobiotic processes leading to gastric or duodenal ulcer.

Facts Which Influence Prognosis.—The theories which have been entertained in the past concerning the formation of the ulcer have received a severe shock from the experimental work of Rosenow, Rosenau and Anderson, which tend to prove that ulcer is of infectious origin. For our purposes in considering the prognosis of both gastric and duodenal ulcer it would be a work of supererogation to consider the many theories which have been advanced. We can only base our prognostic data on incontrovertible facts and these prove that:

(*a*) Ulcer of the stomach is most frequent in anemic or chlorotic women, between the ages of 20 and 40. Sixty per cent of all stomach ulcers are found in women. In these young subjects the stomach mucosa heals readily after injury or abrasion and simple uncomplicated ulcer is likely to heal. The older subjects are much more liable to relapse as the reparative powers are more feeble.

(*b*) While the experiments of Rosenow point strongly to the infectious origin of ulcer, we are not yet ready to accept that theory without question—neither is he—but agree that *ulcer of the stomach is always associated with an acid condition, usually hyperacidity* (Ewald). There may be subacidity.

(*c*) Ulcer of the stomach is a condition which may exist without causing subjective symptoms; such ulcers may heal and the cicatrices are found post mortem in which death was due to some other disease. This fact has been fully corroborated by the observations of Welch who in a large material found that in at least 5 per cent of all deaths there are evidences of ulcers or cicatrices of old and healed ulcers.

(*d*) The *relative frequency* of gastric and duodenal ulcers has only recently been recognized. Gastric ulcer is more frequent in females. The

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Mayo material and that of Moynihan and other observers proves that relatively duodenal is more frequent than is gastric ulcer, and that duodenal ulcer is more frequent in males—77 and 23 per cent respectively.

(*e*) Exceedingly important for diagnosis and prognosis is the established fact that a surprisingly large number of *hyperchlorhydrias are symptomatic* (*possibly provocative*) *of peptic and duodenal ulcer.*

(*f*) *Large surface burns* may be followed by duodenal ulcer. Our experience proves that this is more frequent in children than in adults, that burns with such complications are almost always fatal, that perforation is not frequent but possible.

(*g*) *Duodenal ulcer is a relatively frequent complication of chronic nephritis,* and in two of our cases perforation offered the first evidence of its existence. In some cases the symptoms of duodenal ulcer are in evidence during long periods preceding death from the primary disease, with or without uremia. One of our cases, a physician, with chronic interstitial nephritis, died of perforation with consecutive subphrenic abscess over three years after his initial symptoms of ulcer.

(*h*) Indicanuria does not influence the prognosis. In some cases of duodenal, occasionally with gastric ulcer, we have found it; with perforation indicanuria is usually positive and is simply one of many symptoms, which, if taken alone does not materially influence the forecast.

(*i*) *Peptic ulcer may cause proliferative changes,* induration simulating carcinoma—life may be but little influenced unless there is pyloric constriction or other complications.

(*j*) *Periods of remissions of symptoms without the healing of the ulcer* are to be expected in most chronic cases. The presence of an unhealed ulcer, either of the stomach or duodenum, is always a menace. Such a life is subjected to a number of dangers which without warning may, within a limited period, end it, though the proportion of deaths due to such possibilities is comparatively small. About one-half of all cases will either suffer from recurring attacks or have continuous symptoms. Between 6 and 10 per cent will remain in an uncertain state between recovery and more or less ill health.

(*k*) *The chances of chronicity and marked resistance to medical treatment are almost certain if two or more relapses have been experienced. Our material demonstrates the fact that while the large majority of these do not die directly as the result of the ulcer, they continue unhealed, and with such a history many finally face some one or more of the leading dangers as mentioned below.*

(*l*) *Freedom from symptoms during long periods does not by any means signify cured or healed ulcer.* Failure to recognize this fact with resulting carelessness may provoke one of the grave complications.

So long as occult blood is present in the stool, the ulcer is not healed

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and the dangers of complications exist. A single examination is insufficient, for blood may be absent during limited periods from the stool.

(*m*) *Vomiting.*—The majority of our cases have had irritable stomachs and have often presented with vomiting that has been neglected; most of these cases are relieved by treatment. We do not include a single instance in our series in which life has been lost as the direct result of prolonged vomiting. Cases in which there has been a long period of vomiting with sudden serious complications have had lowered resistance, and recovery was slower than it would otherwise have been. Vomiting is less frequent than one would expect; when it does occur it is likely to recur and continue several days. The vomiting is often paroxysmal; with stricture and dilatation large quantities are vomited at one time at varying intervals.

(*n*) *Examination of Stomach Contents.*—The examination of the stomach contents and the influence of *diet* and *treatment* upon *hyperacidity* where it exists, have an important bearing on the clinical history. Cases in which the excessive production of HCl persists, in which there is almost continuous hyperacidity, often hypersecretion, do not heal as a rule. The more favorable cases for relief of symptoms are those in which there is but slight hyperacidity or in which the symptoms yield to diet and treatment. It will require great caution to interpret the results of chemical analysis of the stomach content in anomalous cases. There are peptic and duodenal ulcers in which there is normal or slightly reduced acidity; cases in which there are exacerbations and both hyperacidity and hypersecretion, and a small class in which with loss of flesh and gradually increasing evidences of cachexia, the acidity falls and lactic acid appears. In this class of cases the development of cancer in the base of the ulcer should be strongly suspected (*ulcus carcinomatosus*).

Gastrosuccorrhea (*Reichman's disease*) should always excite the suspicion of ulcer. Usually it will be found at the pylorus; it may be anomalously located. It is a question whether with reduced resistance and chlorosis, long continued hyperacidity and hypersecretion may not cause ulcer.

(*o*) *X-ray Pictures.—Röntgen rays* are of value for diagnosis; for prognosis they offer but little. Both diagnosis and prognosis can be placed on a solid foundation without the aid of the x-rays, but in doubtful cases, as well as in those cases in which the examination can be made without risk to the patient (transportation, etc.) it should be included in the scientific examination of the patient. X-rays will establish the presence of the hour glass stomach, will make clear secondary gastrectasia, may aid in the early diagnosis (should not be depended upon without other clinical data), will often show hypermobility with ulcer; but hypermobility is not a constant attendant. With duodenal ulcer there is likely to be pyloric insufficiency (Bergman, Friedenwald and Baetjer), causing a prompt discharge of the bismuth into the duodenum

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and the ulcer showing as a small clear spot. Others, including Cole, report the duodenal cap in position, more or less contracted, a "wormeaten" appearance with the duodenal surface of the pyloric sphincter irregular.

Stockton in his recent works says "the radiographic evidence of duodenal ulcer has not yet reached sufficient perfection to warrant making a diagnosis on it alone."

Complications

The leading complications and dangers are:

1. Perforation
2. Hemorrhage
3. Degenerative changes leading to cancer of the stomach
4. Cicatricial distortion and stenosis
5. Perigastric adhesions
6. Exhaustion
7. Parotitis (metastatic).
8. Tetany
9. Acidosis.

1. Perforation. *Perforation at once makes the case surgical.* The full appreciation of this fact will save many lives. The prognosis of perforation depends upon many conditions. While perforation is the most fatal of all the complications of ulcer of stomach and duodenum, it is a fact that in occasional and rare instances nature's protective processes, the unusual resistance of the patient or some factor unknown, may lead to recovery. The busy internist may have two or three such experiences in a life time; they are indeed so rare and unusual as not to be expected and ought not to encourage the attendant in unwarranted delay. One-half of all perforations in women occur between the fifteenth and thirty-fifth year, one-third about the time of puberty (14 to 20). In men there is no time of predilection up to the fiftieth year (Craemer). Perforation is more frequent in men than in women, particularly with duodenal ulcer. Musser in his collective investigation found 28.1 per cent of 1,871 cases with perforation. This is much higher than our statistics from private practice. The German average is in the neighborhood of 13, Lebert and Welch 3 to 6, Leube in 1.2 per cent.

Perforation may be either *partial* or *complete.* The perforation may be prevented or be incomplete leading to *localized perigastritis* or *limited peritonitis* if the adhesions are sufficiently firm to protect the free peritoneum. Brinton in 1858 called attention to the fact which has since been confirmed that most perforations are found in the anterior wall (70 per cent); they are unprotected and complete, and there is resulting *general peritonitis.* This is particularly true of the *acute ulcer.* The *chronic ulcer*

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(Dreschfeld) usually perforates in the region of the pylorus, "on the posterior wall and near the lesser curvature."

The prognosis of perforation of the stomach wall will always be favorably influenced by the physician's ability to make the correct diagnosis sufficiently early (during the first five hours preferably) to lead to immediate surgical action. *Here we have the "acute abdomen" in which there is but scant hope of saving life without radical interference.* The *operation within the first five hours offers enormous advantages* and in the hands of most surgeons, unless there are associated conditions which interfere, recovery may be expected. The forecast is quite different in cases in which diagnosis and operation are delayed beyond the fifth hour. When the abdomen is tense and hard, the pain severe, vomiting persistent, hiccough, rapid and feeble pulse, reduced urine, *blood pressure low after an initial slight rise which usually follows perforation,* the prognosis is exceedingly grave and such cases are rarely saved. When the perforation has existed beyond the time mentioned (10 hours) the features are pinched, the heart rapid, vomiting often fecal, symptoms of extreme toxemia are prominent; neither surgical nor medical treatment offer much chance of recovery.

In apparently perfectly healthy individuals, without a single warning of existing ulcer, perforation may occur and in those above fifty years of age, death may follow within the first few hours, with collapse, before peritonitis develops. If the perforation is small or incomplete and *protective localized peritonitis* seals the opening, recovery will be likely to follow. Such cases are unquestionably more frequent than is generally supposed and post mortems have demonstrated that fact in those who finally died of other disease.

Adhesive perigastritis agglutinating the transverse colon to the stomach wall may serve to protect the peritoneum when perforation takes place, and *gastrocolic fistula* may result. This is always a serious, but not necessarily fatal, complication and may be relieved by plastic operation.

With duodenal ulcer, subphrenic abscess may form, and this without general peritonitis. Perforation from subphrenic abscess into the pleura, lung, or surrounding organs is a serious complication—the early recognition of which may save life. Only rarely does the condition yield without surgical intervention. We have seen two cases. One was associated with *metastatic parotitis* and finally made a slow recovery. The other lived through peritonitis and is now perfectly well so far as we know. In this case, the dense adhesions due to perigastritis saved the man's life. The operation for subphrenic abscess dependent upon perforation is encouraging. Elsberg reports 73 cases—51 were operated and 40 recovered, 18 of 22 not operated died.

Perforation into the pleural cavity or heart sac, into the lung or after long burrowing through the abdominal wall may lead to long periods of

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convalescence, or the patient may, after weeks of symptoms die of sepsis. The heart wall (left ventricle) has been perforated after burrowing, in which the pericardium was naturally first perforated.

The recognition of perforation is not difficult in cases which have offered preceding symptoms of indigestion or ulcer.

The *"acute abdomen"* should be suspected to be due to perforation of the stomach in all cases in which there has been hematemesis, localized pain or other symptoms of ulcer, with the characteristic behavior of the stomach contents (hyperacidity, etc.).

There is no abdominal condition which causes such intense pain, none in which the collapse is more prompt, none in which the physical signs of peritonitis during the early hours are more prominent, and none in which the heart muscle yields more promptly to the resulting toxemia. All of these conditions which mean death, are fortunately less frequently met because of unanimity of opinion by which such cases are immediately referred to the surgeon. Musser agrees that "the best percentage of cures was noted when operation was between one to twelve hours after perforation."

Statistics concerning the results of the medical and surgical treatment of perforation are of little value, and are best omitted because they cannot possibly be based upon premises which are the same in all cases. We do know that almost all die who are not surgically treated. We conclude as we commenced the consideration of this accident that perforation is at once a surgical affair, that delay, failure to recognize the cause of the suddenly arising and severe symptoms causes death; correct and early diagnosis, other factors being favorable, is very likely to save life.

Recovery after operation for *perforation* of either gastric or duodenal ulcer is less favorable in cases with long existing dyspepsia than with a short history of digestive disturbances. The chronic cases with repeated acute exacerbations are found with annoying and complicating adhesions and often troublesome thickening. The *"acute abdomen"* from whatever cause, is serious; the future clinician will meet fewer cases, for experience has grown and the causes which produce it are recognized by the acute diagnostician to receive timely treatment. Mayo (W.) places the conditions which lead to the acute abdomen in the vast majority of cases in the following order of their occurrence:

1st. The appendix.
2d. The duodenum.
3d. Acute pancreatic fermentation.
4th. Perforation of the stomach and of the gall-bladder.
5th. Pelvic conditions which simulate thrombosis of the mesenteric vessels.

2. Hemorrhage.—My experience has brought the usual proportion of ulcers of the stomach but I have lost surprisingly few patients from hemor-

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rhage. Small hemorrhages, or vomitus mixed with blood, are frequent; large hemorrhages are rare, occult blood is practically a constant feature; bloody stools with duodenal, at times with gastric ulcer are to be expected. Statistics are again fallacious because there is no standard of comparison, and those who offer high percentages probably include blood streaks, etc. Welch reported death from hemorrhage in 3 to 5 per cent; Miller in 10 per cent; Muller (L.) in 29 per cent; Ewald and Leube in 1 per cent; and Jacobi's experiences correspond closely with the latter figure. The frequence of hemorrhage is in the neighborhood of 50 per cent.

Leube reports	46	per cent.
Fenwick reports	75	" "
Rutimeyer reports	71	" "
Brinton reports	29	" "

Beyond 50, with high arterial blood pressure and degenerated arteries and gastric ulcer, there may be uncontrollable and fatal hemorrhage. The average mortality from hemorrhage in private practice will not be found above 2 per cent; in hospital practice it may approach a higher figure—6 to 8 per cent.

Repeated hemorrhages with acute exacerbations in chronic cases are ominous. We have seen a number of cases in which there were long periods of remission of all symptoms, in which with recurrence there was the usual localized pain and immediately profuse hemorrhage. Such cases (rare) are likely if they are not treated surgically, during the interval, to bleed to death ultimately. In the hemophilic the prognosis is naturally worse. We cannot too forcibly impress our readers with the great importance of appreciating the prognostic meaning of hemorrhage in this class of cases. Hemorrhage in some chronic cases may prove persistent and causes profound secondary anemia; such cases ultimately prove to be surgical and after a period of reconstruction during a favorable interval, are usually saved by surgical interference. It does not often happen that the initial hemorrhage is sufficiently profuse to deplete and cause death. Such an experience we had only once in a woman of thirty who, after a few days of localized pain and overeating, died within twelve hours following a profuse hemorrhage.

3. Degenerative Changes Leading to Cancer of the Stomach.—When we consider the different opinions and statistics of able clinicians and pathologists relating to degenerative changes, we are forcibly reminded of the fact that the study of gastric and duodenal ulcer offers a series of contradictions.

Zenker in 1882 held that all cases of cancer of the stomach had their origin in simple ulcer. Hauser in 1883 first pointed out histologically the transition of ulceration into carcinomatous proliferation. Haberlin found

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evidences of carcinomatous degeneration in 7 per cent of all ulcers; Miculisz in 7 per cent; Lebert 9 per cent; Rosenheim 6 per cent; Fenwick 3 per cent; Osler 26 per cent; Moynihan 60 per cent; Mayo 54 per cent; Graham 62 per cent; Wilson and MacCarty 71 per cent. Rosenheim came to the conclusion that about one in 15 cases of stomach ulcer develops cancer. Einhorn holds that no one who has had a large experience has found it a frequent occurrence. "This coincidence is so small, cancer being such a frequent malady, that it is doubtful whether ulcer plays a part at all in the development of cancer."

Payr's material of excised ulcers showed cancerous infiltration in 26 per cent. Borrman in a very exhaustive article on the method of growth and dissemination of cancer of the stomach found in 63 cases of ulcer but one in which cancerous degeneration was proved to be present. Reimers, Haberlin, Sonnischen, Haberfeld and Dittrich offer figures between 6 and 22 per cent. Futterer has seen 52 cases in which ulcer led to cancer. Rippert quotes Hirshfeld as saying "the processes are mere coincidence." Borst believes the occurrence is overestimated—he found 5.6 per cent. Wilson, at the Mayo Clinic, in 258 cases of cancer of the stomach found 109 to proceed from ulcers. Friedenwald has made an exhaustive study on the frequency of the transition of ulcer of the stomach into cancer in 1,000 cases of cancer, in 232 of which (23.2 per cent) there was a previous history of digestive disturbance; 73 cases gave a definite history of former gastric ulcer. "It is evident therefore that in the 1,000 cases, but 23 per cent present a history of any previous digestive disturbance whatever, and that but 7.3 per cent give a direct history of ulcer." "If, therefore, all of the former digestive disturbances be considered as due to ulcer, the formation of gastric cancer from ulcer could not have taken place in more than 23 per cent."

Aschoff says that a large number of chronic gastric ulcers, considered callous ulcer by the surgeon, and which have been interpreted as cancer, microscopically are not ulcers degenerated into cancer but cancers in which typical ulcers have formed.

The material which was submitted to MacCarty at the Mayo Clinic was frequently examined within two minutes after its removal from two hundred and sixteen resections of the stomach for ulcer, ulcer and carcinoma, or carcinoma. This material divides itself into three groups—58 ulcers, 125 ulcers and carcinoma, and 33 carcinoma without any good evidence of ulcer. MacCarty under head of "*Ulcer and Malignancy*" says: "The question, do ulcers become malignant as one of their sequelae seems, from my material at least, *to be answered in the affirmative.* What percentage heal, perforate, or become malignant is impossible to determine. The close association of carcinoma with ulcer may be strikingly seen in the fact that *71 per cent of all our resected specimens of the stomach for carcinoma were associated with definite ulcers* (Wilson

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and MacCarty) and that 68 per cent of the resected ulcers of the stomach, including the duodenal ulcer, which rarely becomes malignant, were associated with carcinoma."

Finally Rippert, who is probably the leading authority on human cancer, in his great work says that he has seen three cases of positive cancerous development in ulcer of the stomach, and pictures one of these in his work.

Our own material does not justify the presentation of statistics. We have, because of the great importance of this subject from the diagnostic, prognostic and therapeutic standpoint, presented the most recent data available. For our purposes it may be concluded that on the whole, in spite of the great differences of opinion which exist with regard to the frequency of the degeneration or transition, we must admit that *ulcer of the stomach is a positive factor in the production of cancer*, and prognosis and treatment should be framed accordingly.

In our experience we have never seen a case of duodenal cancer resulting from ulcer.

4. Cicatricial Distortion and Stenosis.—In the process of healing and proliferation the two conditions which are most frequently faced are *pyloric obstruction* and *hourglass contraction* of the stomach. The first condition, *pyloric stricture*, we consider fully in connection with the benign stenoses of the pylorus (See Pyloric Obstruction).

Without complications the prognosis, unless the patient has been exhausted by inability to nourish himself as the result of extreme stenosis, surgery offers an excellent prognosis. Medical treatment is of no avail in extreme cases; with moderate narrowing, life may be prolonged indefinitely with careful regulation of diet. The x-ray picture will prove of material assistance.

The diagnosis of *hourglass contraction* can only be suspected; it can be positively confirmed by x-ray examination in most cases. Consecutive dilatation of the proximal part of the stomach may give rise to all of the symptoms of gastrectasia. The complication is rare. Medicine offers nothing to relieve the symptoms; most cases are not extreme and remain fairly comfortable. Without complication in extreme narrowing, the prognosis for life is good, for surgical interference also good.

5. Perigastric Adhesions.—Most adhesions resulting from ulcer of the stomach do not lead to serious complications or annoying symptoms. Brinton demonstrated their presence in 40 per cent of ulcers. Perigastritis is likely to accompany acute exacerbations of chronic ulcers. With each acute exacerbation adhesions or localized thickening over the ulcer may be expected. This process is at times conservative and salutary, for the local thickening may prevent perforation or limit its ravage.

The adhesions which result to the liver, spleen and intestines lead to pain on movement, particularly bending and stretching. When the new

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tissue is dense and thick there may be tumor formation—at times puzzling for diagnosis.

In rare cases the adhesions may lead to pyloric obstruction with symptoms of motor insufficiency. Adhesions which distort the duodenum may cause regurgitation of bile into the stomach with consecutive symptoms. Most perigastric adhesions require little or no treatment; the deforming, constricting perigastritis demands surgical treatment which offers only reasonable chances of relief. Reformation of adhesions with extensive perigastritis is the rule.

6. Exhaustion.—Exhaustion due to causes other than the serious complications mentioned is at times the cause of death (but rarely). Long continued, uncontrolled vomiting, associated chlorosis and extreme chloranemia, excessive menstruation, irritable or diseased heart, tuberculosis or other diseases may prove factors in causing alarming exhaustion.

The *blood picture* often during considerable periods shows all of the evidences of *grave anemia* which is associated with ulcer symptoms and great exhaustion. This is the complex which exists in young girls very often. Barring accident in spite of the fact that the heart often shows marked muscular enfeeblement and there be slight albuminuria, almost all of these patients recover. It is often surprising to note the extreme exhaustion and anemia even after hemorrhages, and the final restoration of blood elements and strength.

It must not be forgotten that ulcers of the stomach and duodenum are often associated with other diseases which powerfully influence prognosis (nephritis, chronic heart and lung disease, etc.) (Rossle), in which there may be extreme exhaustion.

7. Parotitis (Metastatic?).—In several of our cases we have seen parotitis during the height of the symptoms. Most of these have been found during or after hemorrhage. The swelling is painful; there is the usual rise of temperature and acceleration of the pulse. None have suppurated; all have recovered.

8. Tetany.—We have elsewhere in this volume called attention to the association of *tetany with stomach and duodenal ulcer.* It is always a serious complication and when it recurs demands surgical treatment, which offers a good chance of relief. In some cases in which the ulcer is healed but there is secondary stenosis (incomplete) and motor insufficiency, tetany is prevented by repeated lavage and diet.

9. Acidosis.—There are occasional cases of peptic and duodenal ulcer in which alarming and threatening acidosis develops. *Acetonuria* and *acetonemia* are easily recognized; with acetone there is diacetic acid, and with persistent vomiting and other evidences of poisoning, characteristic breath, small pulse, thready and rapid, features pinched and eyes sunken, respiration is increased and death may follow. This is not the fate of all ulcers with acidosis, for in some during periods of exacerba-

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tion, there is only moderate poisoning. The fact remains that cases of extreme hyperacidity and hypersecretion in which there is uncontrollable vomiting are most likely to develop acidosis.

Contrary to the usually accepted theory of destruction of the liver cells and excess of ammonia in the urine, it has been suggested by Underhill and Rand that the excess of ammonia ought not to be attributed to the degeneration of liver cells but to the direct results of starvation dependent upon uncontrolled vomiting.

Dreschfeld has called attention to attacks of fainting with acetone and diacetic acid. We have had such cases in which threatening acidosis never developed. Rational treatment influences the majority of moderate acetonemies favorably and promptly. The deep involvement of the sensorium, rapid respiration, extreme weakness and small pulse are serious—not necessarily fatal. We have had a number of satisfactory recoveries.

Important Considerations

We have in private practice found ulcer of the stomach in 1.4 per cent of our cases of internal disease with a mortality of less than 2 per cent. The mortality of simple and complicated gastric ulcer with surgical treatment would naturally be high, as the average would be lifted by emergency operation for perforation or for any complication. Musser compiled reports from literature and various private sources; his results include a large number of operations during the pioneer days; they varied between 10 and 25.9 per cent.

It is unfair to offer an opinion in the individual case based on statistics which cannot possibly be considered to include parallel conditions nor equal skill or resourcefulness of the various operators. Hence statistics bearing on this subject will probably never be of great value, save as they prove the possibilities in the hands of the expert and the average results of all operators. The mortality for simple ulcer after surgical operation varies from less than 2 per cent (Mayo-Moynihan) to 10 per cent and more, and it has been demonstrated that operations for duodenal ulcers present a higher average of cures than operations for gastric ulcers.

Prognostic Significance of Age and Surgical Treatment

Petren has demonstrated, in an investigation of 243 operated cases collected, that it appeared that younger subjects did not show as favorable late results as did older individuals. In 33 women under 30 years who had been operated, 42 per cent had subsequent gastric disturbances. In 33 women over 50 years of age, only 24 per cent had subsequent trouble; and out of 41 men over 50, only 17 per cent had any annoying symptoms.

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It is exceedingly difficult to offer any statistics of value which bear upon the relative frequency of the complications of simple peptic or duodenal ulcer. Much must depend upon early treatment and care. The average statistics of ten years ago are of no value today, for medical dietetic and surgical treatment have all been improved and it is as unjust to the physician as it is to the surgeon to make comparisons which are not based upon conditions which exist at the present time.

The mortality based on surgical treatment will always be higher than that offered by the internist, but in all fairness to the surgeon we must admit that this is so because the average surgical material even of simple uncomplicated ulcer includes only the more serious and chronic, oft-relapsing cases which have during long periods postponed treatment and operation, or the acute cases with symptoms of sufficient severity to demand an emergency operation. Musser's analysis of cases from medical literature and a collective investigation of private cases (1,871 and 586 respectively) shows that in simple ulcer the death rate under surgical treatment was 20 per cent and under medical treatment 12.4 per cent (reported in 1907 from literature). The private cases showed a surgical mortality of 11.4 per cent and a medical mortality of 3.1 per cent. After my full rehearsal of the prognostic features of gastric and duodenal ulcers I feel safe in advising the clinician to consider the majority of these cases to be purely medical offering a good prognosis for life and cicatrization.

There never is a time when the patient with an unhealed chronic or acute ulcer is not standing on the edge of a precipice ready to fall, never a moment when without warning his condition may not become surgical, though the large majority escape serious complications. Ulcers which are chronic and which prove their chronicity by repeated remissions and exacerbations with or without hemorrhage do not heal—the complications which threaten life will complicate a small proportion of these but chronic invalidism is their positive fate, and as the exacerbations multiply, adhesions and secondary changes (perigastritis, stricture of the pylorus, dilatation of the stomach) will prove increasingly annoying—at times threatening.

Death resulting from ulcer during its incipient stage (acute ulcer) occurs in about 1 to 2 per cent. These figures approximately correspond with those of Russell.

Duodenal ulcers rarely heal; they do not cause cancer. The question of surgical interference to prevent cancer from ulcer will need to be decided in the individual case.

Gastric ulcer may cause cancer but the incidence is not as frequent as the statistics of some clinics appear to prove; sufficiently frequent, however, to influence prognosis and treatment. The prognosis of complications has been favorably influenced by the growth of physiologic

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and pathologic knowledge and the enormous improvement of surgical technic.

In threatening complications, perforation particularly, life often depends on prompt diagnosis and immediate surgical treatment.

Rest, diet and medical treatment are the paramount factors which the physician possesses to aid him in the cure of most cases or the control of symptoms.

We must once more accent the fact that all threatening acute cases and all chronic relapsing cases, as well as life threatening complications demand the concerted action and ripe judgment of both the physician and surgeon—and this without delay. These facts accepted and acted upon, the mortality of gastric and duodenal ulcer will be enormously influenced and will be found to be surprisingly low (below 1.5 per cent).

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7. Cancer of the Stomach

(*Carcinoma ventriculi*)

General Considerations.—On the basis of past statistics Hoffman concluded that during 1913, 30,105 would die of cancer of the stomach and liver; and his forecast was practically corroborated.

The annual mortality in the United States from cancer, Hoffman places at 75,000; 500,000 in the civilized world. Cancer death rate is increasing at the rate of 2½ per cent per annum, and this holds throughout the civilized world. The average age of death from cancer is 60.4 years for males, and 58.2 years for females.

The male cancer death rate in the United States at ages 25 and over has increased 29 per cent during the last decade, and the female cancer

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death rate has increased 23 per cent. The cancer mortality in Japan ranges from 83 to 95 per 100,000 inhabitants; Moscow 56 to 103; St. Petersburg 78 to 98; Southern Italy 6 to 70; Northern Italy 51 to 68; in the Netherlands 75 to 105; Germany 33.5 to 35. In the United States in 1907 it was 79.6 per cent in the cities, 73.9 per cent in the country. Rosenfeld reports the interesting coincidence brought out by his figures that the mortality from cancer is unusually high in the district of Joachimsthal, the source of the radium supply. The study of "cancer-free islands" is of great interest; there are no "cancer-free islands" in countries in which cancer is prevalent. Rosenfeld accents the fact that "there are numerous cancer islands in countries which are generally free from it."

The rule may be accepted without modification that *cancer of the stomach is always a fatal malady unless detected in its very incipiency before marked infiltration has resulted, before adhesions have formed, before neighboring glands have been involved, and before there are evidences of changes in the blood.*

There is no reason for considering the majority of stomach cancers to be other than primary, therefore, no valid reason for concluding that cancer of that organ, if radically treated, during its early days differs from primary cancer elsewhere which offers a favorable prognosis only under the conditions mentioned in the preceding paragraph.

There are powerful factors, however, which make the *early recognition of stomach cancer* exceedingly difficult and usually impossible save by exploration. The stomach is a tolerant organ; it continues to perform its functions during relatively long periods in the presence of organic disease which it continues to tolerate without creating a suspicion of its presence. The intestinal and pancreatic functions compensate for the failure of full gastric digestion, while the patient, in most cases, in the presence of few symptoms of "dyspepsia" is but little disturbed by these, and usually fails to seek medical assistance; when he does, in the very early days of the disease, the diagnosis remains, as already said, difficult and uncertain.

We are reminded that the consideration of these tests, together with clinical history, should make early diagnosis easy: the *analysis of the stomach contents,* the *testing of the motor function, the x-ray examination, the Solomon test* (determination of the amount of nitrogen contained in a known quantity of water with which the stomach is washed out—because with cancer there should be an increased amount of serous fluid discharged—more than normal, hence an abnormally high nitrogen content), the *Graefe-Röhmer hemolytic test,* and the *Oppenheimer test.* Unfortunately all of these do not accomplish the desired end.

The thorough investigation of the Solomon, Graefe-Röhmer and Oppenheimer tests by Leitner prove that all of these have inherent

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sources of error which make the results uncertain and unreliable (Leitner). *The early diagnosis of cancer by the Röntgen rays is uncertain* and according to the most reliable authority (Haudek), carcinoma arising from a callous ulcer, a fungus carcinoma which has invaded the normal stomach outline, a *diffusely infiltrating cancer, may make it possible to determine the character of a cancer with tolerable accuracy.* These are all advanced conditions and have nothing in common with incipient carcinoma ventriculi; in all of these, the revelations of the x-rays are tardy and can only corroborate, when made, an unfavorable outlook because of the advanced changes.

The repeated examinations of the stomach contents may make us suspicious, but they offer during the earliest stage but little upon which we can rely. Billroth in a personal communication to the author on this subject shortly before his death wrote: "It is true that free HCl is more often absent from gastric juice in gastric cancer than in ulcer; but this phenomenon is not sufficiently constant and may be physiological. It is not sufficiently definite to be of practical value." Billroth added: "I consider the differential diagnosis of an ulcer of the stomach with cicatrization and beginning carcinomatous infiltration from primary cancer as very difficult and usually impossible, ofttimes impossible when the fresh specimen is before us and cut into, only possible after many and large sections have been made and examined microscopically." We have mentioned these facts as a preface to what follows because they demonstrate the problems which confront the clinician if he would improve the forecast of the disease under consideration. The patient, if he would be saved, must consider his symptoms with his attendant early and the physician must learn to associate these symptoms with possible malignant disease of the stomach. Patients will never learn to present for early diagnosis until we have made clear to them, as we have to the incipient tuberculous, the facts relating to carcinoma which make prognosis favorable. Therefore, we repeat, *early diagnosis is the only hope of the patient who has stomach cancer.* Depend upon laboratory methods or any one symptom for diagnosis and your patient's death warrant has been signed. The pyloric portion of the stomach is the seat of cancer in over 70, Mayo says 80 per cent of stomach cancers—therefore in the majority. The earliest evidences of motor insufficiency and stagnation (at the cancer age or earlier), food remnants after seven hours with pyloric resistance, and tumor, are the most dependable of all symptoms; all other data are of secondary import. In over 90 per cent of our cases there was a palpable tumor at the time of the first consultation. This fact proves that symptoms are absent or insignificant and treatment is not demanded until the process is well advanced.

To the above we add the Leube rule, which should be indelibly impressed on every diagnostician:

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"Cancer of the stomach is present in all probability if a questionable stomach disease has attacked a patient between 50 and 60 years of age who formerly digested all food well. If such a person becomes dyspeptic without an evident etiological factor, it may be assumed with considerable certainty that he is developing gastric cancer."

"Cancer during early life is by no means exceptional, and this fact cannot be ignored in either diagnosis nor prognosis. The average percentage of stomach carcinoma in early life is between 2.5 and 4 per cent. Osler reports in 3,257 cases of stomach cancer 2.5 per cent below the age of 30 years. Welch in 2,028 cases found 2.5 per cent below 30.

Stomach cancers in early childhood are exceedingly rare. Rolleston and Hague report 17 cases collected from medical literature. One was an infant 10 days old, reported by Cullingsworth; Welch considered the growth to be congenital.

Between 10 and 20 years of age cancer of the stomach is likely to be more acute than in the adult and usually runs a rapid course. After 20 until 30, reported cases show rapid progress to death. Mathieu in a series of 19 cases in young subjects, also quoted by Osler and McCrae, estimated the duration at three months. Eleven of Mathieu's cases lived 2½ months; 6 lived 6 months and 2 one year. *Latent periods are not to be expected in the cancer of early life.*

The scirrhus cancer is the most frequent; colloid second; encephaloid third, and always of rapid growth; epithelial fourth; and adenoid fifth. Welch in 1,885 reported that "it is probably fair to conclude that in New York not over 1 in 200 of the deaths occurring at all ages from all causes is due to cancer of the stomach, and that about 1 in 100 of the deaths from 20 years of age upward is due to this cause."

Our statistics show the larger number of stomach cancers in male subjects. Welch believes the liability of the sexes is the same. *Heredity* is certainly a factor—less frequent than has been supposed (15 to 20 per cent). It is not uncommon to find several members of a family with cancer of the stomach, a fact which is confirmed by the experience of the average busy clinician. It is an interesting fact that in most of these the symptoms appear at about corresponding ages.

Secondary stomach cancer is rare, but possible. Welch's material included 17 secondary to cancer of the breast. We have seen similar cases, and in one woman we found first uterine cancer for which she was successfully operated, later breast cancer also successfully operated, and finally stomach and liver metastases.

The negro is rarely afflicted in his native country (Africa), while in the United States the proportion of deaths—as determined by Welch in an analysis of "7,518 deaths among this race in New York"—was about one-third less than among white persons.

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Prognostic Significance of Leading Symptoms

Pain.—Pain usually present, is not a symptom of great prognostic value; the rule may be accepted that pain is not, as a rule, an early symptom, that its persistence is evidence of advanced disease.

Vomiting.—Vomiting is absent from one-eighth to one-fifth of cancers of the stomach (Lebert and Brinton). In such cases there is no consecutive constriction at either end of the stomach. When the cancer is located at the cardia, it may lead to all of the symptoms of esophageal stricture, the vomiting or regurgitation follows promptly after taking of food. Dilatation, pocketing of the esophagus, with contraction of the stomach follow after a few months of symptoms and progression. *Vomiting is present in practically all cases in which the pylorus is the seat of disease* (80 per cent). The greater the quantity vomited at one time, the more dilated will the stomach be found and the greater the obstruction. *Vomiting of blood, hematemesis*, is not an early symptom except in cases in which there is infiltration of the base (ulcus carcinomatosum) of an old ulcer. These cases, often run a chronic course and are often slow to develop metastases. The *"coffee ground" vomitus* is evidence of advanced change in the growth (degeneration and ulceration); usually there is marked emaciation, cachexia, anemia, and muscular enfeeblement at the same time, with a failing heart (small pulse) and evidences of distant metastases. Under these conditions life is not prolonged.

Once there has been marked *emaciation* there is but small chance of improvement; progression is manifest in the daily loss of strength and the increase of stomach symptoms.

Stomach Function.—Stomach function is always disturbed in the presence of cancer. In the latent cases the reduction may be so slight as to remain unnoticed—no symptoms or but few; the tolerant stomach is relieved at the same time by the compensatory action of the pancreas and intestines. This ability of the stomach, when the pylorus has been removed to regain sufficient motor ability that the duodenum may carry on digestion, is the prime factor in the prognosis of early radical treatment of pyloric cancer. Miculicz and Rosenheim found that in three months motor function was sufficiently restored after removal of the pylorus to empty the stomach of its contents in five hours and a half; the duodenum and small intestines assume the stomach's work. Ninety per cent of our cases show a reduction of free HCl. In average cases pepsin will be present, but reduced in accordance with the destruction of the peptic glands. *Lactic acid* is likely to be present; it is not pathognomonic. Lactic and other organic acid with reduced HCl, the Boas-Oppler bacillus, blood and mucus are presumptive evidence of gastric cancer. The yeast fungus is present in advanced carcinoma. When bits of cancer tissue are vomited the disease is advanced, and ulceration or breakdown is progressive. When

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the vomitus has a gangrenous odor, sloughing and sepsis go hand in hand. Such cases often have *fever* and may show marked toxic symptoms (cerebral) as the end approaches.

The *condition of the bowels* is of no great significance unless there is persistent diarrhea, when the effect is weakening; usually constipation is troublesome.

Stomach Contents.—The diagnosis of cancer of the stomach once established the condition of the contents, whether there is absence or presence of HCl, is only of slight prognostic value. The cases in which there is subacidity (not complete absence) do sometimes run a longer course than do those with complete anacidity (absence of the HCl), particularly if there be *achylia gastrica,* which with carcinoma is indicative of far reaching infiltrating disease and atrophy of the gastric follicles. The cases with persistence of free HCl are usually, not always, *ulcus carcinomatosum* and these are likely to be chronic with latent periods to be mentioned later. The presence of lactic and other organic acids (butyric, acetic), with the Boas-Oppler bacillus and yeast, is usually significant of advanced carcinoma and probable motor insufficiency (stagnation). Golding Bird in 1843 demonstrated the absence of free HCl in pyloric cancer with dilatation but his communication was ignored until von den Velden at the Kussmaul Klinik systematically investigated the subject and established its diagnostic value. Free HCl is the remnant which is left after all affinities have been satisfied. With *"the constant presence of free HCl made positive after repeated examinations and a normal peptic strength" it will rarely be necessary to consider cancer of the stomach.* Riegel would not consider the diagnosis of cancer under such conditions "however strongly they (the symptoms) point to it." The greater the infiltration the more likely are we to have reduced HCl and the worse is the prognosis—this is particularly true when at the same time there is little pepsin and no peptones.

Cancer of the pylorus may be limited, always fatal when advanced and yet free HCl is usually present, "its absence is the exception" (Cahn and von Mehring). This ought not to be accepted as a rule. Free hydrochloric acid was absent in 92.7 per cent of my cases; present, but markedly reduced, in 7.3 per cent.

The Glycyltryptophan and the tryptophan tests have been fully considered by Smithies who reports on 1,400 cases of diseases of the stomach examined at the Mayo clinic. From these we can draw no data which influence prognosis or make positive the early diagnosis of cancer of the stomach.*

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* The tests are known as the Fischer-Neubauer glycyltryptophan test for the presence of polypeptid splitting ferments and the Weinstein tryptophan test for the presence of free amino-acids.

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Smithies found the first mentioned test present in 31 of 81 stomach cancers, the tryptophan test was positive in 7; with 35 ulcers 9 showed Fisher-Neubauer test and 3 the Weinstein; with 87 duodenal ulcers 3 and 3 respectively. Other diseases—benign pyloric stenosis hypoacid anacidity, gastritis, neuroses and achylia gastrica, also gall-stones, cancer of liver, appendicitis, and pernicious anemia—gave positive results. No other disease gives so many positive reactions as does cancer of the stomach but in the absence of other suggestive or classic symptoms and positive Fischer-Neubauer and Weinstein with the knowledge that other diseases with similar symptoms give the same results, we are left without any material assistance from these tests. Feurer says "We can only consider the tests (including the Salowski—colloidal nitrogen, the hemolytic bodies, the Graefe—Röhmer and the Neubauer-Fischer tests) of value when the clinical features are corroborative", and when these are, the disease is advanced far beyond the period of incipiency or even the first stage.

Blood Picture.—The blood picture is of value in giving a fair estimate of the ability to nourish the patient. With progressive loss of strength, weight, and increasing secondary anemia and cachexia, life is threatened. With average infiltration the *cachexia will always be out of proportion to the anemia*—of diagnostic as well as prognostic value. My average red count at the time of positive diagnosis has been 3,500,000 per c. mm.; hemoglobin 50 with leukocytic range between 10,000 and 15,000. In some cases, where there is excessive vomiting the count may temporarily approach a polycythemia. This is rare, however.

Fever.—Persistent fever, usually 100°–101½° F. is not infrequent; it is almost always evidence of the terminal stage of the disease. But few cases die without rise of temperature at some time during the course of the disease. When fever persists it is an evidence of absorption of toxins and it is an unfavorable symptom. *Chills and fever* are always suspicious of sloughing and consecutive sepsis.

The *behavior of the heart and circulatory organs* is of value in giving an index of the patient's resistance as well as deciding in conjunction with physical signs and subjective complaints on the probable duration of life.

The Urine.—The urine offers but few data. The *chlorids are reduced;* there is usually, particularly in the advanced stage, *indicanuria;* there may be *nephritis* or *albuminuria.*

I examined the urea content in all of my cases and have learned that advancing cases, during limited periods, often show very high urea loss. *The urea estimation in all suspected cases is valuable for diagnosis and prognosis. When the disease is advanced the amount of urea is diminished. Acetonuria,* if slight is not, *per se,* of great significance, it may cause no symptoms; when it does and the symptoms of *acidosis* are prominent the danger is great.

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Dropsy.—Most cases are either edematous before they die, or there are evidences of dropsies of the serous cavities, or both. Dropsy is always an evidence of the approaching end. With dropsy there is usually marked cachexia and anemia; most dropsical patients have died with symptoms of toxemia, more or less delirium, and final coma.

Ulcerative Stomatitis and Dry, Red, Glazed, Cracked Tongue.—Ulcerative stomatitis and the dry, red, glazed, cracked tongue are among the terminal conditions. I have never seen a case fall into a period of latency or remission after the tongue shows decided change.

Perforation.—I have had no death in my practice due directly to perforation of the stomach wall. In one case there was perforation into the adherent transverse colon (gastrocolic fistula) which was at first unrecognized because, as the stomach was inflated, the distension of the colon simulated dilatation of the stomach. This patient lived a number of months after the perforation. There are a number of cases of peritonitis on record following perforation, but this combination is relatively rare.

Latency of Gastric Cancer

In 1893 I called attention to a series of cases which justified the conclusion that latency of stomach cancer is not unusual. There may be after symptoms strongly suggestive and sufficient for tentative diagnosis, marked improvement during varying periods, gain of strength and flesh, improvement of stomach function, approximate return of normal gastric juice, favorable change in the blood picture—all sufficient to create the suspicion of faulty original diagnosis. In some cases the motor function as shown by tests has increased. In these cases it may be assumed that stenosis does not exist to any high degree and that the intestines, and the duodenum particularly, are sufficient to nourish the patient. These cases are therefore without much constriction at the pylorus or secondary dilatation, or there is infiltration with only moderate thickening at the pylorus. The length of the periods of latency varies, the longest period in my experience being 6 years; during the early stage there were characteristic symptoms. This was not a case of cancer upon the base of an old ulcer as was proved by the post mortem. Death followed 12 months of continuous symptoms. There are cases in which cancer remains latent, never causing subjective symptoms and is detected post mortem, death having been due either to accident or intercurrent disease.

The blood picture of stomach cancer is not characteristic, but in this class of cases there may be less cachexia than is usual. As the process advances and the powers wane the cachexia is relatively greater than the anemia. The unfavorable features which show progression and presage an early ending are those of increasing stagnation, dilatation with periodic vomiting, progressive loss of flesh, increasing cachexia, and secondary

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anemia. In these cases after the long period of latency, the tumor is usually palpable.

Infiltrating cancer without palpable tumor, cases in which the stomach wall is evenly invaded, may not cause stagnation. The pylorus may not be constricted; if it finally is, then there will be stagnation with moderate dilatation and progressive, often rapid emaciation.

With infiltrating cancer which may be mistaken for non-malignant atrophy of the gastric follicles, there will be remnants of the previous days' food, usually absence of HCl; lactic acid will be present; there will be progression of the disease, never improvement of functional activity of the stomach. Whenever the cancerous growth fails to cause stagnation, the prominent symptoms may mask the primary disease. Such patients often die with the secondary manifestations in the ascendency. In some cases death may follow with the secondary lesions of liver cancer prominent, but few or no stomach symptoms.

Metastases

Both latent and infiltrating carcinoma may present symptoms of metastases before local evidences or subjective symptoms of existing disease. The most frequent metastases are to the lymphatic glands (in $\frac{1}{3}$ of all cases), to the liver in an almost equal number, and to the peritoneum, omentum and intestines in approximately $\frac{1}{4}$ of all cases, the pancreas in $\frac{1}{8}$, the pleura and lung in 1-15. We have called attention to metastasis to the nervous system from cancer of the stomach and intestines. The secondary growths may be more conspicuous in causing symptoms than the primary. There may be invasion of any part of the nervous system, peripheral, spinal, or cerebral. Welch reported 9 metastases to the brain and meninges in 1,574 cancers of the stomach. Pinatelle and Cavaillon report 2 cases of gastric cancer with secondary deposits in the cranial bones.

Additional Considerations

Long periods of latency or remission of symptoms alone can justify the belief during limited periods, that gastric cancer is curable. If the disease is carcinoma, relapse and death are sure to follow. *The cases of so-called "self-cure of cancer" are usually ulcer with thickened or fibroid base—never cancer.* I fully agree with Mayo when he makes the following positive statements: "In all the history of disease there is no authenticated case in which a cancer of the stomach has been cured by medical means." Accepting this view, as absolutely true, we once more find ourselves face to face with the problem of early diagnosis and prompt surgical interference if we would save the lives of these patients. It is not within the province of this work to deal with surgical questions, but only benefit can result from the presentation of a few data taken from the

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material of those in whom we may place reliance that the prognosis of the disease may be improved and cancer of the stomach may from the very beginning of observation of the individual case demand the attention of the diagnostician and the surgeon. Mayo reports: "Cancer of the stomach, when still localized, gives operative results as good as those after operation for cancer in any other part of the body; it has no higher grade of malignancy nor is the operation for its removal more difficult than operation for the cure of cancer in other organs of the gastro-intestinal tract."

It is obviously unfair to compare results today with those of even five or ten years ago—so great has been the improvement of technic—and so much better educated is the public that results are growing more and more favorable; the mortality is steadily diminishing. I was present at the Billroth clinic during the early days of the work in which he was the pioneer, and I have recently had opportunity to compare it with modern surgical methods in this country and abroad. The revelations are encouraging and prove the courage of the master who paved the way as well as the fact that the mortality of all plastic operations on the stomach depends not only on the early diagnosis but upon the cool judgment and superior skill of the surgeon. In no field of medicine does prognosis depend more upon the experience—the most valuable asset of the operator. Mayo reports a mortality of 7 per cent in his last 100 cases; in the last 50 of these, 4 per cent. He modestly adds: "nor are these figures exceptional." In this latter conclusion we differ from him; he underestimates the value of his experience in the cases preceding his last 50. No patient can be considered cured who has not remained well five years.

"Of 307 resections of the stomach for known carcinoma 150 of the patients were operated more than three years ago; 20 died from the results of the operation, and we were unable to trace 40. This gives 90 patients who recovered from the operation and whose present condition we have been able to trace. Of this number 33 or 36.6 per cent are alive. Of the 93 patients operated more than five years ago, 15 died and 20 have not been heard from as to their present condition. Of the remaining 58, 13, or 22 per cent, are known to be alive and well over five years. Every death occurring within the five year period has been classed as a death from return of the cancer without regard to the actual cause; this is an injustice to the statistics, since the normal death rate for five years of people the age of these patients is at least 8 per cent." These results prove that "in the operated cases 90 per cent chance of recovery from the operation exists, a 36 per cent chance of 3 years of life, and 25 per cent of 5 years."

Faroy reports as follows on his surgical experiences with cancer of the stomach:

Exploratory laparotomy was done on 8 cases, 6 of which died soon after operation (3, 19, 23 and 30 days) from postoperative complications; 2 survived, 1 six

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months, the other 1 year, in spite of the presence of ganglia, adhesions and infiltration of the gastric wall and gastrohepatic ligament.

Gastro-enterostomy—39 cases;

8 survived only from a few hours to several days.
11 " up to 6 months (2, 3, 4 and 6 months).
9 " more than 6 months (7, 9, 10, 11 and 12 months).
9 " from 1 to 2 years.
3 " for 1 year 3 months.
2 " " 1 " 5 "
2 " " 1 " 10 "
1 " " 1 " 11 "
1 " " 2 years.
1 " more than 2 years (2 years 6 months).
1 " " " 3 " 3 " 4 "

Of these patients 9 had pyloric or prepyloric cancer, and survived as follows:

Several hours 2
3, 6 and 7 months..... 3
1 year, 1 month..... 1
1 year, 10 months..... 1
1 year, 11 months..... 1
3 years, 4 months..... 1

Fifty per cent did not live one year; 45 per cent lived more than one year. Of 30 other cases of pyloric and prepyloric cancer and cancer of the lesser curvature, 77 per cent did not live one year, 23 per cent more than one year.

In 12 cases the neoplasm was extensive, had infiltrated the glands or contracted adhesions with the liver and pancreas:

2 died after several hours.
2 " " " days.
5 " before 1 year (7, 8, 10 and 12 months).
2 " " 2 years (13 and 23 months).
1 lived 3 years and 4 months in spite of pancreatic adhesions.
25 per cent did not live 1 year; 30 per cent not more than 1 year.

Pylorectomy.—Simple pylorectomy (*Billroth's method No.* 1) shows different figures from gastro-enterostomy.

Of 10 patients, 5 died soon after operation from complications: 3, 7, 15 and 30 days.

5 survived: 1 year 6 months.
1 " 9 "
2 " 2 "
3 " 4 "
4 " 6 "

One patient in whom a total gastrectomy was done survived 3 years in spite of extensive lesions.

Billroth's method No. 2 gave similar results.

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Of 6 patients, 2 died 10 and 15 days after.
4 survived: 10 months.
1 year 1 month.
1 " 4½ months.
1 " 10 "

If we combine the figures of these two groups we find 7 deaths out of 16—a postoperative mortality of 45 per cent. The mortality in the cases operated according to Billroth's method No. 1 was 50 per cent, that of method No. 2, 33 per cent.

Temoin reports that the following results were obtained in 11 years, from 1898 to 1909, on 168 tumors of the pyloric region. Of this number, 91 were operated before 1908, and 77 in 1908 and 1909. Of the first 91 cases, 38 are dead, 24 dying within 5 days after operation and 14 within 15 days. Of those operated in 1908, 44 cases, 4 died within the first 5 days and 3 within 15 days. Of those operated in 1909, 33 cases, 2 died within the first 5 days and 3 within 15 days.

The figures show a uniform decrease in the immediate results of the operation, due to the ability of the operator and improved technic.

Of the 119 that survived operation, 47 are still living and in good health:

1	operated	in 1898	13	years.
1	"	" 1899	12	"
1	"	" 1901	10	"
4	"	" 1902	9	"
5	"	" 1904	7	"
3	"	" 1905	6	"
4	"	" 1906	5	"
5	"	" 1907	4	"
8	"	" 1908	3	"
15	"	" 1909	2	"

"Setting aside the 15 survivals since 1909, that is 2 years ago, a sufficient length of time for recurrence, we still have 32 without any symptoms of relapse."

The oldest living case was one in which the tumor had so far advanced that exploratory laparotomy was done, and in spite of the objections of the attending physician Temoin removed the growth. This was 13 years ago and the man is living, works and eats everything. Examination showed the growth to be a carcinoma.

The greatest number of the cases operated were between 45 and 55 years; the youngest, 22 years, died 2 years later from metastases in the liver; the eldest, 71 years, died 27 months later from generalized cancer of the peritoneum.

Federman offers the conclusions of the Germans; they are:

Resection is justified so long as the growth has not extended beyond the stomach or has not invaded the liver or pancreas. The size or seat of the limited growth are no contraindications. The author contends that the pessimistic views entertained are not justified, for from 20 to 30 per cent of operated cases are permanently cured.

Complications

Among the complications besides metastases are *thrombotic processes,* jaundice, not due to the secondary deposits in the liver, i. e., catarrhal jaun-

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dice, gall-stones, pancreatic invasion by continuity, pressure on the bile duct, pancreatic duct, the portal lymphatic glands and the liver itself (Welch). Chronic gastritis, non-malignant peritonitis, enteritis, colitis, nephritis, pericarditis and after perforation pyopneumo-thorax, abscess or gangrene of the lung.

Hypostatic congestion of the lung was found at post mortem in a number of the more chronic cases.

Tuberculosis may accompany cancer; it is not a frequent complication. *Healed tubercle nodules are not at all infrequent. Purpuric and embolic conditions* are always terminal manifestations of malnutrition.

Barring cases with latent periods, *the average duration of life was fourteen months.* Schweppe reports an acute case of twenty weeks' duration. *Encephaloid cancer* has run its course in less than three months. Boas reports five weeks' duration of an acute, probably encaphaloid growth.

Much depends on the extent, rapidity and location of the growth as well as the dissemination of the metastases, the individuality and the resistance of the patient as well as the complications. *Hemorrhages* are rarely sufficiently profuse to shorten life though they have a depressing effect on the patient. The mortality of cancer of the stomach will be reduced and life prolonged when we have educated the layman and the profession to appreciate that in all doubtful cases which justify the suspicion, exploratory incision is imperative and radical surgical intervention is demanded when the infiltration is found to be limited, is without distant metastases or more than local glandular invasion. It must be remembered that a small and symptomless nodule in the stomach may cause metastasis to a distant organ.

"Cancer of the stomach is the most frequent and the most hopeful form of cancer in the human body. Early operation affords the victim the only chance of cure" (Mayo).

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8. Hematemesis—Gastrorrhagia

Hematemesis (or vomiting of blood) and gastrorrhagia (or hemorrhage from the stomach) are not absolutely synonymous. A patient with gastrorrhagia may have hematemesis, or vomit blood, while the patient with hematemesis may vomit blood which does not come directly from the stomach.

Extragastric Bleeding.—Extragastric bleeding which leads to hematemesis is, as are all bleedings, purely symptomatic and may be due to a variety of causes. It not infrequently happens that the *tuberculous patient with a profuse bronchial hemorrhage* swallows considerable blood and finally vomits it; the same is true of *profuse epistaxis.*

I mention hemorrhage from *esophageal varix with Banti's disease,* also with other esophageal lesions (ulceration, etc.). *Decubitus esophageal* ulcer may lead to hematemesis also *specific, tuberculous* and *esophageal peptic ulcer,* low down. With *chronic valvular lesions* and *portal destruction,* varices or profound engorgement of the esophagus may cause extragastric bleeding.

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Aneurismal ulceration, usually aortic, with final rupture into the esophagus is a cause of death. The bleeding may at first be slight, but suddenly it becomes profuse and is promptly fatal. Tumors within the thorax or abdomen may by pressure cause hemorrhage.

Intragastric Hemorrhage.—With *splenomegaly* due either to leukocytic leukemia, splenic anemia, pernicious malaria, pernicious anemia, or other grave diseases there may be gastrorrhagia; it is always threatening and may either deplete the patient if profuse and cause death or it may materially shorten life.

Banti's disease without esophageal varices may cause profuse gastric hemorrhage due to profound engorgement of the vessels of the stomach, gastric varix or hemorrhagic diathesis (purpura).

Cirrhosis of the liver is one of the most frequent causes of hematemesis. *Amyloid degeneration of the mucosa, acute yellow atrophy of the liver* and *surgical lesions* are also included as causes of hematemesis.

Chronic hyperemia of the gastric mucosa from whatever cause, circulatory disturbances as a rule, including chronic valvular and myocardial lesions, may cause gastric bleeding.

Hemorrhage from ulcer and cancer of the stomach is separately considered. The former may threaten, occasionally does destroy life; the latter is rarely sufficiently profuse to interfere materially with the course of the disease; it is, however, an expression of disorganization and advanced disease (See Cancer and Ulcer of the Stomach).

With the *infections,* gastric hemorrhage is experienced. These include *smallpox, measles, typhus and typhoid fever, relapsing fever, acute yellow atrophy, embolic infarct with sepsis*—indeed, any infection with purpuric or embolic processes or profound and disorganizing constitutional disturbances may be responsible for hematemesis.

Various *poisons,* metallic and vegetable, food poisoning (phosphorus, etc.) may lead to moderate, at times, profuse stomach bleeding.

Hemophilia, the *severer purpuras,* at times *chronic purpura,* are factors, the recognition of which for rational treatment is all important.

Following abdominal operations, more frequently than others, particularly if the omentum is injured, gastric hemorrhage may follow. With such complication there is usually peritonitis, and the prognosis is grave. I have seen gastrorrhagia with intestinal obstruction.

Hysterical hematemesis is not frequent; it may occur but is never serious. *Simulation in unexplainable cases should be considered; its detection has often proved exceedingly difficult.*

Hematemesis or gastrorrhagia, always symptomatic, the influence can only be considered with the underlying cause in the individual case. *The intragastric hemorrhages* rarely lead to death directly; they are not usually profuse unless a large vessel has been eroded. The *extragastric conditions* are more likely to cause profuse and fatal hemorrhages (aneurismal

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rupture, traumatism, large varices, etc.). Epilepsy may occasionally cause transitory insignificant gastrorrhagia.

Hemorrhage from the stomach with the *infections* is usually an evidence of malignancy of the infection, and is of grave import. *Septic conditions with multiple hemorrhages including gastrorrhagia are generally fatal.*

Occasionally there is *oozing from the gastric mucosa without known cause;* this condition occurs in girls near puberty, without pain or other subjective symptoms. The condition is not often serious though it may, if persistent, lead to secondary anemia. It is known as gastrostaxis. *Purpuric or hemorrhagic conditions in the newborn* with hemorrhages from mucous membranes is almost always fatal. We have seen petechiae and cord infection with these cases.

9. Gastric Neuroses

(*Nervous Dyspepsia, Dyspepsia nervosa* (*Leube*)

General Consideration.—The consideration of dyspepsia is now limited entirely to those forms of (1) *sensory,* (2) *motor,* and (3) *secretory* anomalies in which no anatomical change in the stomach can be diagnosticated or detected post mortem. All of the neuroses are characterized by poor and deranged digestion, in which the leading symptoms and general character of the disease point to the ungeared nervous system as the seat of the trouble. I consider with neurasthenia and hysteria many of the features of nervous dyspepsia (See separate chapters on Neurasthenia and Hysteria), and must here again accent the facts that in all there is an unstable nervous system, a strong neuropathic habit; the *ego* is usually in the ascendency, and the patient is so self-centered that he is unable without powerful assistance to divorce himself from himself. He is eager to will but he cannot; his symptoms are almost continually before his mental vision, and with all forms of the disease the importance of each feature is enormously exaggerated. There is no other organ of the body which is so often the seat of symptoms of a functional character as the stomach.

With all of the neuroses there may be psychoses which include manic-depressive types, hypochondriasis or other anomalies. The *phobias* (fears) or *imperative conceptions* (obsessions) are often in the foreground and there is a strong tendency on the part of the patient to become more and more inefficient with the severe complex. *There are but few patients who suffer from nervous dyspepsia who are not neurasthenic.* In some cases there is organic disease with which dyspepsia is associated. Basedow's disease, anemia, malaria, uterine and ovarian anomalies in women, genito-urinary disturbances in man, suprarenal disease and spinal lesions

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are often burdened with nervous dyspepsia. Ocular anomalies unquestionably prove provoking factors. Often the graver disease is forgotten in the presence of symptoms referable to the stomach.

1. Sensory Dyspepsia—Hyperesthesia

The leading features of the sensory neuroses are subjective. With normal, perverted or lost appetite, at times a craving for unusual foods, the *marked general hyperesthetic condition* of the patient stands out in bold relief. Often the *fear of eating*, causes loss of flesh and strength. The gastric mucosa revolts as soon as food enters in some cases. The resulting pain is described as unbearable, usually burning, boring, lancinating, or there may be complaint when the stomach is empty. These patients react peculiarly to medicines and foods. At times they show great tolerance for indigestible foods, while at the same time they complain of the acute pain which follows the simplest diet.

Gastralgia, so called "neuralgia of the stomach" in my experience is rarely of functional character. I do not agree with Cohnheim that the neuroses of the stomach are not associated with pain or "neuralgia," but I hold that gastralgia is so rarely of functional origin that the diagnosis should not be accepted until all of the features of the case have been thoroughly considered. The diagnosis should be made with a "loop hole" attached, through which the diagnostician will usually be forced to escape. *Recurring gastralgia* should always create the suspicion of gall-stones, tabes dorsalis, ulcer of the stomach or duodenum, chronic appendicitis, bone or other pressure (spinal or aneurismal).

The *mental condition* of the dypeptic with this form of the disease is out of all proportion to the importance of his neurosis. As in all other forms of nervous dyspepsia the majority of patients are women. In some of these cases hyperacidity has been demonstrated; in the majority of cases the examination of the stomach contents offers nothing.

Psychic influences, distant irritation, eye strain, a general condition below par, sexual anomalies, long continued worry, lack of occupation or overwork, occupation which is not suited to the individual, are all factors which make it impossible, unless relieved, to throw off the load which overwhelms the patient. The outlook in the cases which can be removed to the needed environment, with the relief of the neurasthenic and irritating factors, the added strong personality and overpowering suggestion of the attendant who is not wedded to polypharmacy, but who takes advantage of rational and natural methods of treating these unfortunates, is relatively good. These factors are important and influence the forecast of all types of gastric neuroses.

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2. Motor Gastric Neuroses

Motor disturbances may be due to (a) *hypermotility* or (b) *hypomotility.*

(a) **Hypermotility** (*Supermotility—Hyperkinesis*). The prompt and premature expulsion of the food from the stomach may cause no subjective symptoms, may be associated with the neurasthenic accompaniment, and can only be recognized by the use of the stomach tube or x-ray.

The *peristaltic unrest of Kussmaul* is due to the contraction and relaxation of the stomach musculature following the taking of food. In these cases there may be hypersecretion and hyperacidity. The attending nervous symptoms are prominent; vomiting is not infrequent; migraine is at times annoying; belching of gas, splashing noises, abnormal rapid emptying of the stomach, at times *pylorospasm,* all are without pain. In all of these cases the suspicion of organic disease should not be surrendered until there has been a thorough and satisfactory differentiation. Stockton and others have called attention to the possibility of pyloric and cardiac spasm in the same patient. *Pyloric spasm* long continued, as well as *cardiospasms* may lead to serious malnutrition.

With hypermotility, the *loud and annoying belching of gas* (*aërophagia*) is often uncontrollable during days at a time. In most of these, positively without organic fundament, the noisy and active belching ceases during conversation or distraction. We have seen a number of cases in which the symptom yielded to hypnotic suggestion; in occasional cases a sudden shock or intercurrent illness had a salutary effect. The expelled air has been aspirated or swallowed.

Nervous Vomiting.—Hypermotility may cause so called *"nervous vomiting."* In most of these cases there is a powerful hysterical or neurasthenic element which is materially aggravated by the persistent emesis. Between the separate emeses there may be peristaltic unrest or almost continuous belching of gas. The element of suggestion is prominent. The stomach, as shown by x-rays, is often filled with gas; the stomach content is found normal—occasionally there may be hyperacidity. There is never in uncomplicated cases the presence of organic acids.

Rumination—Merycismus.—Rumination in the human being is exceedingly rare. In my practice it occurred only twice. In both instances the patients were neurasthenic during long periods with ultimate permanent psychasthenia. Cases in the hysterical and insane, epileptic and idiotic, are occasionally recorded. When it becomes a habit, as it does very rarely, it is exceedingly rebellious to suggestion and is probably a stigma of degeneracy.

(b) **Hypomotility.**—With atony of the stomach wall (musculature) the organ does not empty itself normally; there is stagnation, with final dilatation, and in some cases tetany (See Tetany). These patients are

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highly neurotic; their *splashing stomachs* and eructations are to them enormously significant; they develop all manner of nervous symptoms; are exceedingly unhappy and often suffer from insomnia, and as most patients with gastric neuroses, they are subject to the *cardiac neuroses, palpitation, precordial distress* and *abnormal fullness.*

Insufficiency of the Pylorus.—In some of these cases the pylorus is insufficient—a condition which is not usually recognized. When *gastric atony* persists unrelieved, the general condition suffers and there is always justification for the belief that it is dependent upon an organic fundament.

3. Secretory Anomalies—Reichmann's Disease

Hypersecretion and hyperacidity may be of functional character. Reichmann first called attention to this combination which is now recognized by the use of the tube and examination of the stomach contents. The presence of abundant hyperacid gastric juice in the stomach, when it should be empty, is characteristic. Long continued *Reichmann's disease* leads to motor insufficiency, in some to complete gastric atony. *Gastralgia* is a prominent symptom after great excitement or emotion. In all of these cases organic disease of the nervous system, ulcer, or other anomalies should be considered and strongly suspected.

Hyperacidity (*Hyperchlorhydria*).—Hyperacidity may be diagnosticated when the total acidity of the stomach contents is continuously above 60. Not all who have a total acidity of 60 or slightly above show symptoms, but with neurasthenic symptoms and stomach distress such figures do justify the diagnosis. I am always suspicious in the absence of organic stomach disease and hyperchlorhydria of gall-stones or cholecystitis, and such suspicions have often been confirmed by the subsequent history. The presence of hyperacidity continuously not dependent upon organic disease, besides a train of nervous manifestations which are common to all the gastric neuroses, is likely to cause sensory disturbances, pain, gastralgia and (as the condition is found in young girls at puberty) often there is marked chlorosis. *Epigastric pressure, pyrosis, eructation of some fluid* and *vertigo* are the leading symptoms besides the marked neurasthenic features.

Anacidity or Reduced Total Acidity (*Hypochlorhydria*).—Anacidity is characterized by the abnormal lowering of free HCl in the stomach contents. This condition is exceedingly rare in functional disease. There is an *achylia gastrica nervosa.* Riegel says: "It cannot be denied that occasionally achylia gastrica may be merely a perversion of function."

Long continued achylia or hypoacidity unless recognized and compensated by diet and treatment leads to loss of weight and strength. In some cases which have been originally considered functional, the advent of pernicious anemia has cleared the horizon.

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In presenting the leading clinical features of the various gastric neuroses the psychic element has remained prominently in the foreground. Dreyfus has, after a thorough consideration of his material concluded that practically all forms of nervous dyspepsia depend upon psychic changes, and that the stomach symptoms are of "secondary nature." Pawlow's observations prove conclusively the close relationshop of the psychic and nervous element with gastric function. What is said in connection with the prognosis of neurasthenia and hysteria is equally applicable in offering the forecast of all gastric neuroses. The prognosis of most of these functional anomalies is good when we have gained an insight into the prime factor which has caused and is continuing the symptom complex. This means the thorough analysis of each case, the differentiation which when complete will materially reduce the number of these cases, and the regulation of the lives of these patients that gladness may displace the gloom which surrounds them. Besides the strong personality of the attendant to lead the patient, the healthy occupation of the mind will do more than anything else to bring relief and cure. *Uncomplicated gastric neuroses do not lead to death. Recurrence in all forms is the rule.*

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G. Diseases of the Intestines

1. Acute Enteritis—Acute Diarrhea

(a) *Acute Catarrhal Enteritis*

Acute catarrhal enteritis—catarrh of the bowels—is one of the most frequent of all acute diseases; it is most frequent in young subjects, oftener during the first two years of life. The disease may be either *primary* or *secondary*.

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When acute diarrhea is *primary,* it is due to some error of diet, polluted food—ptomain poisoning—impure drinking water, epidemic conditions, excessive heat, with at the same time the eating of spoiled or tainted food (milk usually) toxic agents, drugs, such as arsenic, phosphorus, corrosive sublimate, purgatives, mental emotion, particularly fright.

The *secondary* causes are the *infections,* heart diseases in which there is acute congestion of the mucosa, disease of the lung, acute or chronic congestion or obstruction in the liver, trichinosis, intestinal parasites, diseases of adjacent organs, extensive surface burns, nephritis, malaria, and the various cachexias.

Acute duodenitis, or catarrhal inflammation which limits itself to the duodenum, which may or may not be associated with gastritis usually causes *jaundice* (See Catarrhal Jaundice). The latter condition is also known as *gastro-duodenitis.*

Diarrhea is not necessarily an attendant of all catarrhal enteritides. It may be absent with duodenitis or inflammation of limited portions of the small intestine; such conditions may cause *constipation.* The more severe forms may involve not only the lower half of the small intestine but include the large intestines and provoke painful and weakening diarrhea with tenesmus and heart weakness. Most of these recover after from ten to twelve days.

The simple uncomplicated primary form of the disease without jaundice is easily controlled, and without more than a few days of weakness after the control of the diarrhea leads to full recovery without sequel. In some cases the recovery may be protracted, particularly when the cause is not at once evident or the intestinal tract has not been freed. When the *mesenteric glands* are involved, recovery is slow. If there are *catarrhal ulcers* there may be a subacute course, but such cases are exceptional. Only rarely in average treated cases does chronic enteritis follow.

Idiosyncrasies cause some to develop diarrhea (acute enteritis) when certain foods are taken which have no influence on normal individuals. These cases are easily controlled by diet. *Food poisoning* is elsewhere considered in this work. *Enteritis due to ptomain poisoning* is often severe and weakening, and when the patient is overwhelmed may prove very serious. Naturally the prognosis depends on the quantity and virulence of the poison, the prompt relief by vomiting early or late, and the ejection of the poison before it has been absorbed. The more unfavorable cases are those in which symptoms are postponed from twenty-four to forty-eight hours after the taking of the poison (See Food-poisoning).

The *prognosis of the secondary enteritides* depends entirely upon the ability to influence the underlying causes; if these are remediable, as in malaria, some forms of acute nephritis, circulatory faults, intestinal parasites, relief is possible.

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(b) *Croupous Enteritis—Diphtheritic Enteritis*

Diphtheria may cause croupous enteritis with characteristic diphtheritic sloughs and ulcerations, and in rare cases perforation may result. The ulcerations are most frequent in the large intestine.

Croupous enteritis may follow or be associated with *mercury poisoning,* profound *uremia, chronic nephritis,* and *dysentery,* and may develop upon *specific tuberculous* or *septic ulcers* (Matthes).

Riedel has reported diphtheritic necroses in the jejunum and ileum after laparotomy in weakened individuals. These conditions are all associated with weakening and uncontrollable diarrhea besides tenesmus and tormina. When croupous ulcerations of the intestines complicate the infections (pneumonia, pyemia, typhoid, smallpox and sepsis) chronic nephritis, cirrhosis of the liver, cancer or the other primary infections mentioned in the preceding paragraph, enteritis may be only superficial, without serious moment; on the other hand, it may prove to be among the terminal symptoms.

(c) *Phlegmonous Enteritis*

Phlegmonous enteritis with ulceration is not frequent. It may be associated with *streptococcus infection* (*erysipelas*), *surgical lesions of the intestines,* such as *intussusception, volvulus, strangulated hernia, traumatism, or any of the mechanical obstructions.* Unless the primary source of infection is relieved death will surely follow. These cases present a dark outlook.

(d) *Ulcerative Enteritis*

Ulcerative enteritis is usually *secondary* to the infections, including *syphilis, tuberculosis, typhoid fever, dysentery, splenic fever;* to the *constitutional* diseases including *leukemia, purpura, amyloid disease, arteriosclerotic changes,* and *infarct;* also to neoplasms and conditions which originate outside the intestines, which by continuity lead to ulceration and perforation; *decubitus ulceration* is occasional.

Acute and chronic catarrhal follicular ulcers may form after acute or subacute uncomplicated catarrhal enteritis has existed for some time; this is more likely to happen in children than adults and may prove rebellious to treatment, though the majority heal, leaving recognizable cicatrices. Ulcers may exist in adults during long periods without causing symptoms. Multiple ulcers of the intestine due to enteritis or infection may in the process of repair and final cicatrization lead to *single or multiple constriction of the intestine,* usually incomplete, but sufficient to cause symptoms of partial obstruction and chronic invalidism. The differentiation of this form of ulceration and tuberculosis is often exceedingly difficult. I have in such cases found the patient incapacitated during many years with

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almost continuous symptoms. In one such case following typhoid fever, an exploratory laparotomy disclosed multiple constrictions with collapse of intestines below the first narrowing in the jejunum and marked pocketing above. There were eight separate constrictions. This patient lived unrelieved during four years after the exploration, and died of asthenia. When the ulcerations are in the large intestine (rectum, sigmoid, etc.) of specific catarrhal or dysenteric origin, they are amenable to treatment and many make very satisfactory recoveries (See Syphilis, Dysentery, also Actinomycosis).

(e) *Mucous Colitis—Membranous Enteritis*

The prognosis of mucous colitis depends entirely upon its cause. All cases may be divided according to their etiology into:

(I) Nervous or hysterical colitis
(II) Infectious mucous colitis
(III) Infantile mucous colitis
(IV) Secondary mucous colitis.

(I) **Nervous or Hysterical Colitis.**—I have elsewhere considered mucous colitis of hysterical or nervous origin (See Hysteria, Neurasthenia). The condition is most frequent in women but is not infrequent in men. It is usually one of many symptoms which are evanescent, and its importance is almost always enormously exaggerated by the patient. The passage of mucous casts always has a depressing and discomforting effect on the patient, though in truth the strength or resistance of the patient is not disturbed by it. The disease is chronic; it does not as a rule yield to medical treatment but is materially influenced by psychic impressions, rest and changed environment; it may disappear suddenly and permanently without known cause, or relapses may be frequent. In some cases there is associated and weakening pain. We have never known of serious complications or death from hysterical or nervous membranous enteritis—a fact which it is necessary to suggest repeatedly to these patients; once indelibly impressed, the result is wholesome.

(II) **Infectious Mucous Colitis.**—In children with intestinal infection, casts or membranes occasionally form in severe summer *diarrheas*, which are weakening and threatening. This complication is not frequent. In some of these cases the Shiga organism is present. With *croupous enteritis in adults*, without diphtheria bacilli, casts may form; unless the constitutional symptoms are severe or the enteritis deep with ulceration the prognosis is good. With acute infectious enteritis mucous casts may form, and are found in the stools. The prognosis in these cases is good. Catarrhal and infectious enteritis in hysterical subjects may be complicated by membrane formation, without materially influencing the progress of the acute inflammation.

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(III) **Infantile Mucous Colitis.**—The *infectious infantile colitis,* at times *enterocolitis,* has been mentioned in the previous paragraph; it may complicate *cholera infantum* or it may be due to faulty feeding and persisting intestinal catarrh and indigestion. In young children, colic and membrane formation may occur without known cause, though as a rule there are evidences in fever, rapid pulse, and constitutional symptoms of acute infection. The association of membranous colitis with the diarrheal diseases of childhood, in weakened rachitic and underfed children may prove serious. Most of my cases have made full recoveries, and a similar experience in over 95 per cent of all uncomplicated cases may be presaged.

(IV) **Secondary Mucous Colitis.**—In grave organic diseases such as the deep ulceration of *carcinoma, tuberculosis, syphilis* or *decubitus ulcers,* membranes may form, are cast off in the stools with pain—at times tenesmus—characteristic of the primary disease. The prognosis of the underlying condition is almost always unfavorable, the addition of membranous enteritis is not of grave import.

(*f*) *Cholera morbus—Cholera nostras*

During the summer months sudden, acute, severe abdominal colic associated with diarrhea and vomiting, some fever, acceleration of the pulse dependent upon the eating of unripe fruits, bob veal or other errors of diet is frequent, but in the previously healthy is promptly relieved by simple means, often without medical treatment and without sequelae. In the very weak and sick, severe cholera morbus may, during collapse cause ominous heart weakness, but death very rarely. In previously normal adults I have never known of a death. From twenty-four to sixty hours finds the patient fully restored, barring a slight remnant of weakness.

I do not classify the infections due to the Gaertner bacillus (bacillus enteritides) as cholera nostras (See Food Poisoning) neither can we in this country accept the statistics of Rumpf (quoted by Matthes) that 10 per cent of cholera morbus patients die in collapse. If we include the food poisonings above mentioned, we might possibly approach that mortality. In all doubtful cases the diagnosis will require the differentiation of Asiatic cholera (during epidemics), acute poisoning (arsenic, phosphorus, strophanthus, etc.), intestinal obstruction, gall-stones, appendicitis, perforative peritonitis from stomach more likely duodenal ulcer, and nephritis with uremia.

2. Chronic Enteritis—Chronic Diarrhea

Neglected or severe acute catarrhal enteritis may occasionally cause chronic changes in the intestinal mucosa and mesenteric glands. The

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changes may be atrophic, or there may be cystic degeneration of the intestinal follicles as described by Aschoff (colitis cystica). Chronic hyperemia of the intestinal mucosa, dependent upon circulatory or respiratory disease, chronic nephritis (uremia) or constitutional disturbances, may cause chronic diarrhea. *In children, chronic diarrhea with wasting, may be associated with tabes mesenterica* (tuberculosis of the mesenteric glands), or in earliest life to what was formerly supposed to be an atrophy of the intestinal glands, but which has been found to present no structural changes (Aschoff, Huebner, Schelbe and others) and is now characterized as *enteropathia dyspeptica chronica.* In the foregoing conditions the prognosis depends entirely upon the ability to nourish the patient and compensate by proper diet for the loss of normal intestinal digestion.

The classification of the chronic diarrheas of the adult is, thanks to the thorough study by modern methods of the stool and the association of symptoms with microscopic finds made possible, and the prognosis therefore rests on a solid foundation (Schmidt and Strassburger).

Intestinal dyspepsia, dependent upon fermentation, in which there are symptoms of catarrhal enteritis, persists until the fault (usually faulty starch digestion) is corrected by diet and other treatment. The diagnosis and prognosis of these cases may be cleared by the examination of the stools which are light yellow, contain gas bubbles, are mushy, have a sour odor, and give an acid reaction. Macroscopically there are abundant remnants of undigested potato; microscopically after staining with iodin the starch cells are in the ascendency undisturbed, surrounded by microörganisms. Schmidt and Strassburger found fermentation of the stools in the incubator. These patients digest albumin and fat well. Unless the condition has been present during a long time, with a suitable diet, these patients may be freed of their intestinal indigestion and chronic diarrhea.

The second variety of chronic diarrhea which Schmidt classifies is the *gastrogenic diarrhea.* In these cases it may be assumed that stomach digestion is at fault. The stools on a meat diet show by the presence of the meat and connective tissues, shreds particularly, that gastric function is impaired. With these diarrheas, anacidity, atrophy of the gastric follicles or functional indigestion may be paramount (achylia). The entire failure of stomach digestion in these cases to supply the intestine with its normal stimulant is largely responsible for the symptoms. In some of these cases the hypermobility of the stomach is a factor, for not all patients with achylia have diarrhea. These *gastrogenic diarrheas* may be dependent upon a variety of causes and may include at the same time intestinal anomalies. Matthes suggests that in the absence of a single fault in the stomach which accounts for all cases, it might be wise to characterize them as *chronic gastro-intestinal dyspepsia.*

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Chronic diarrhea may be of nervous origin and it is not uncommon in such cases to find *alternation of constipation and loose bowels.* Schmidt relegates a few of these to faulty pancreatic function, *functional pancreasachylia.*

Most of the *nervous diarrheas* are largely dependent upon psychic influences, are not easily influenced by diet or medicine, and are favorably affected by travel, environment and agreeable occupation.

I mentioned the prognostic significance of chronic or persistent diarrhea with exophthalmic goiter and Addison's disease (See Diseases of the Ductless Glands). With both, weakening diarrhea contraindicates surgical interference and influences the case unfavorably. Often the symptom improves with the other manifestations, and gain of flesh is phenomenal. There are individuals, usually of nervous organization, who are unable without resulting diarrhea to take certain foods, milk particularly. Such idiosyncrasy does not make wholesome diet impossible, and with compensation for the loss of one or two articles of food, weight is improved and enteric symptoms are relieved.

Chronic enteritis may result from previous typhoid infection, from dysentery, paratyphoid infections, chronic malaria, and any disease which causes atrophic or productive changes in the intestines. Such cases are favorably influenced by diet; death rarely results as the direct effect of the enteritis.

There are veterans of the Civil War still living with chronic diarrhea which resulted from acute infections of the small and large intestines during service. In these chronic cases there is always danger of the *opium habit;* among some of the veterans above mentioned the "black drop" is still taken.

Habitués of opium are often the victims of secondary diarrhea, and *paresis of the intestinal musculature may cause symptoms of obstruction. Chronic ulceration of the intestines, from whatever cause, may continue diarrhea.*

Secondary Chronic Diarrhea

Chronic nephritis, uremia, cirrhosis of the liver, heart lesions, tumor pressure, secondary chronic hyperemia, and *amyloid disease,* may all continue diarrhea during periods of varying length, according to the nature of the primary disease and the ability of the patient to resist.

Chronic lesions within reach of the eye (rectal, sigmoid) which are non-malignant, with modern methods of recognition and local treatment, offer a good prognosis if not too far advanced.

Productive changes and distortions secondary to dysentery are purely surgical affections; strictures of the rectum or sigmoid may continue chronic diarrhea, as may also chronic constipation and malignant constrictions. Frequent, small stools, often unsatisfactory stools, should always

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create the suspicion of an unrelieved bowel, just as frequent unsatisfactory urination, is evidence of retained urine.

Diagnosis and prognosis of all forms of chronic diarrhea are materially advanced by the repeated consideration of the *general condition of the patient,* for in unexplained diarrhea suspicion should fall upon several vital organs, including kidney, liver, heart and nervous system.

Sprue

(*Chronic Enteritis of Warm Countries, Aphthae tropical, Aphthae orientales, Psilosis linguae et mucosae intestini*)

With sprue the entire mucosa of the intestinal tract is involved in a chronic and remitting inflammation which seems to attack Europeans mainly, living in tropical or subtropical climates. The tongue and mouth are mainly involved in superficial ulceration; the mucosa is hypersensitive, while the intestinal lesions cause diarrhea. The disease is occasionally brought to our country; in the tropics it may complicate other forms of enteritis. Thin has suggested the name of "psilosis" because of the raw appearance of the tongue and intestinal mucosa. Manson says: "Of all the chronic diseases the European has to contend against (in South China), sprue, in its various forms and degrees is by far the most frequent as well as the most formidable."

The bacterial cause of sprue is uncertain. Whatever its cause finally proves to be, the peculiar history of the disease, its chronicity, long periods of latency and recurrence (patients without returning to the source of infections years after the initial symptoms, developing anew the symptoms) will require consideration. Unless relieved, the loss of flesh and strength with anemia and heart weakness associated with the "primary and secondary effects of starvation" (Manson) may cause death. The organic changes in the intestines, gastric mucosa, as well as in the upper portions of the alimentary tract, may be deep and variable. They include follicular changes, ulcerations, atrophy, infiltration of the mucous membrane (leukocytic), and in the more chronic types, fibrotic or productive deposits throughout the small and large intestines.

When the disease is limited to catarrhal changes, full recovery is possible. The deeper changes above mentioned are secondary in all probability to long continued and unrelieved catarrhal processes, and while symptoms may be partially overcome, the organic changes remain. In all the cases seen in this country, the *tongue lesions* have been prominent and painful. These cases, unless relieved, progress; emaciation advances and is excessive; the patients resemble the reconcentrados of the Cuban War; the urine is albuminous, edemas and general dropsy follow with increasing uncontrolled diarrhea, death results from starvation. The prognosis depends entirely upon removal to proper quarters and proper

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food during the early stage of the disease—before the mucous membrane of the alimentary canal has been destroyed. The clinician should not be deceived by periods of marked improvement or latency; he must guard his prognosis because of the tendency of relapse even after years of freedom as already suggested (See references for history and literature).

3. Diarrheal Diseases of Early Childhood

I have repeatedly in the preceding pages referred to the infections of the infant which lead to diarrheal diseases, and have considered their prognosis. The campaign of education which has led to clean and pure milk has done much to reduce infant mortality. He who practiced during the days when ignorant of the causes of intestinal diseases thousands of infants were annually sacrificed, and who is privileged to note the change which has followed the dissemination of knowledge among the masses and the medical profession, is deeply impressed by the favorable advance.

Prophylaxis is possible in all communities and in all families wherever concerted action of the profession and responsible head of the house obtains. The reduction of infant mortality from diarrheal diseases is the problem of the state and the municipality. Infant mortality will be reduced to an almost negligible factor when ideal conditions prevail. What they are, the profession understands; it remains only for the profession to demonstrate these to the lawmakers that competent health officers may cooperate with every household.

Besides the prophylactic factors which can be easily controlled, the baneful effect of *humidity* and *high temperature* on infant mortality due to diarrheal diseases must be considered; to these factors must always be added bacterial contamination (the Shiga bacillus usually). The change which has resulted in infant mortality is best understood when the mortuary records of large cities are considered. Naturally the death rate is lower from cholera infantum and other diarrheal diseases of early life during favorable summers. In London, as in all cities, the science of infant feeding has progressed and the mortality during all years since 1906 has been materially reduced. The last (1910) census of the United States shows for the registration area as a whole, the general death rate was 15 per 1,000 population for 1910, including an element due to infant mortality amounting to 2.9 deaths of infants under 1 year, and 4 deaths of children under 5 years per 10,000. There were 44,695 deaths of infants under 1 year of age from diarrhea and enteritis. The previous census, 1905, published in 1907, shows that in 1905 the death rate from diarrheal diseases was higher than during the preceding four years.

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CENSUS OF 1905.

Age	Number of Deaths from Diarrhea and Enteritis					
	Annual Average 1900–1904	1901	1902	1903	1904	1905
Aggregate deaths.....	36,021	35,596	33,627	33,035	36,864	39,399
Under 2 years.....	29,183	28,523	26,903	26,697	30,315	33,032
2 years and over.....	6,838	7,073	6,724	6,338	6,549	6,367
	Number of Deaths per 100,000 of Population					
	Annual Average 1900–1904	1901	1902	1903	1904	1905
	112.8	113.8	105.4	101.6	111.3	116.7
Under 2 years.....	91.4	91.2	84.3	82.1	91.5	97.8
2 years and over.....	21.4	22.6	21.1	19.5	19.8	18.9

The census of 1910 shows that over 90 per cent of all deaths from diarrhea and enteritis were in children under 5 years, and 70 per cent were of children under 1 year of age. The total number of deaths of infants under 1 year for 1910 was 154,373—one-fifth of all deaths (19.2 per cent). During the second year 33,080, or 4.1 per cent of the total. Of 58,089 deaths of infants under one month 5,901 were due to diarrhea and enteritis. Beginning with the second month of life diarrhea is the most serious cause of infant mortality. Of 15,223 deaths of infants 1 month of age and under 2 months, 4,692 were from diarrhea and enteritis. Infants 2 months of age and under 3 showed 4,980 deaths from diarrhea and enteritis.

DIARRHEA AND ENTERITIS (Under 2 Years of Age).

	1909 No. of Deaths	Death rate per 100,000 Population	1910 No. of Deaths	Death rate per 100,000 Population
The registration area.....	44,648	87.8	54,216	100.8
Registration cities.....	30,504	102.9	36,781	117.8
Registration states.....	38,033	85.9	47,197	98.7
Cities in registration states.....	23,889	103.6	29,712	118.0
Rural part of registration states.....	14,144	66.7	17,485	77.3
Registration cities in other states....	6,615	100.4	7,069	117.1

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The above statistics make reliable comparisons from year to year impossible because the registration of births in the United States is defective.

The rate of infant mortality as given by English and continental cities where the registration is practically correct are encouraging. The following from the annual summary of the Registrar-General of England:

The decrease per cent between 1881-1885 and 1906-1910: in London 24.0, Edinburgh 6.3, Paris 34.6, Amsterdam 55.7, St. Petersburg 6.8, Berlin 41.3, Hamburg 32.4, Munich 42.6.

The features which make the prognosis of cholera infantum bad are weakness and lack of resistance, collapse, high temperature, rapid pulse, profuse watery depleting stools, convulsions, great restlessness, dry tongue, reduced quantity of urine, tenesmus and uncontrollable vomiting. . With irregular respiration and opisthotonos the prognosis is also bad; also with *bronchopneumonia or other complications.*

Enterocolitis, ulcerative enteritis and membranous enteritis of childhood are considered in the preceding pages of this chapter. The mortality of summer diarrhea is always higher when the Shiga bacillus and streptococcus are present. The mortality in the presence of the gas bacilli, averages between 40 and 60 per cent in large cities. When acid movements are improved by proteid food the prognosis is accordingly better.

Schmidt's bile test in the summer diarrhea of infants has been thoroughly tested for its prognostic value by Pearson. It has been established that zymotic enteritis (infectious) is associated with a marked diminution in the secretion of bile; in the cases which come to the post mortem room, according to Pearson, the tests for bile remain negative throughout the intestines. In a series of 500 cases with the "proper secretion of bile restored, and no other complication—such as bronchopneumonia—the cases invariably recover." In Pearson's latest publication he says: "The point I wish to lay stress on is that in over 2,000 cases of acute summer diarrhea (of infants) I have never lost one in which the Schmidt test * continued, or after treatment became positive. With as much emphasis I may say that I never managed to cure one case in which the test continued negative."

4. Celiac Disease—Diarrhea alba—Diarrhea chylosa

In children between the first and third year without the appearance of organic change, there may be numerous large, foul-odored, light col-

* Schmidt test: A teaspoonful of fecal matter is placed in a wide test tube, a little sterilized water added, and well stirred with a glass rod. The tube is then filled to four to six times the volume with a saturated solution of corrosive sublimate, the mixture well shaken and allowed to stand twelve hours. By this time feces if normal becomes colored bright red, showing the presence of hydrobilirubin or stero-bilin, but if unchanged, bile pigments are present and the color becomes green. If no change occurs bile is absent.

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ored stools, resembling porridge. These children lose flesh and strength progressively; there is marked muscular weakness; in some there is threatening, at times, fatal tetany, and a number of writers have found *infantilism* result. This type is exceedingly chronic, and improvement is often followed by repeated relapse and death. The fault lies in the failure of the child to digest fat and starch, and unchanged fat is found in the stools. These cases may be so severe as to suggest *tuberculous enteritis* and *tabes mesenterica.* In rare cases there have been ulcers. The substitution of raw minced meat or meat juice, improves most cases.

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5. Enteroptosis

(*Glenard's Disease*)

See Diseases of the Stomach—Section V, F-4.

6. Constipation—Obstipation

Constipation is as a rule a functional disorder, for which the patient is largely responsible. It is a physiologic fact that different people differ as to the frequency of bowel movement. There are women (rarely men) who continue perfectly well with one movement every two to four days. In most cases chronic constipation leads to or is associated with more or less disagreeable symptoms, mental depression, languor, drowsiness, inertia, anorexia, foul tongue and breath—and in young girls particularly—*anemia,* with other *toxic symptoms. Individual predisposition* is an important etiologic factor, as is also *heredity.*

Habits and *diet* are paramount and their correction, almost at once re-

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lieves the *atony* which continues constipation. *Sedentary habits are productive of intestinal inertia.*

Faulty diet includes an excess of one article to the exclusion of many others. *Sweets* (candy), *starches* in excess, are leading faults which cause constipation. *Insufficient fluids* (water) and *fats* will often continue constipation until the deficiency is supplied.

Procrastination is one of the prominent causes of constipation. The habit of moving the bowels at the same time each day is easily and promptly formed even in chronic cases.

Mental emotion, long continued worry, circulatory diseases, gastro-intestinal diseases including the neuroses, also *central nervous diseases,* as *brain tumor, spinal lesions,* compression of the spine (caries and tumor), are all provocative.

The *mechanical obstruction* of the intestine at one or more points is not true constipation, but is considered with intestinal obstruction—either partial or complete. Pregnancy is a frequent cause of constipation. *Chronic constipation may be diagnosticated when the bowels refuse to move without assistance, either by medicines or mechanical means.*

In all forms of obstipation in which correction of existing faults fail to overcome the symptoms, organic disease should be strongly suspected. Thorough search will usually reveal either a rectal anomaly, uterine or other pressure, or some positive cause, either intestinal or remote. Among the conditions which are often overlooked as causes of *obstipation* are chronic intestinal catarrh, lead poisoning, general asthenia and the functional gastric neuroses. *Secretory anomalies,* without organic change, when corrected, either in the stomach or intestines, cure constipation dependent upon them.

The atonic form of constipation is dependent upon (*a*) *reduced intestinal peristaltic activity,* or (b) there is *insufficient expulsive strength* which includes enfeebled action of the diaphragm and abdominal walls.

(a) *Reduced Intestinal Peristaltic Activity.* — Reduced intestinal peristaltic activity may follow long continued fevers or non-infectious diseases. It depends largely upon neural disturbances. It is frequently an expression of the neurasthenic complex—hysteria, inertia, central disease—and in the majority of cases is due to improper stimulation of the intestinal mucosa because of the faults mentioned in the preceding paragraphs. In most cases in which reduced intestinal peristaltic activity is the paramount factor the regulation of the life of the patient, including proper exercise, diet and regularity in the attempt to move the bowels at the same time each day, though not at once successful, will always in the end prove efficient and if continued cure the bad habit. *Neglect will provoke recurrence. Rectal torpor* is a frequent and unrecognized cause.

(b) *Insufficient Expulsive Strength.*—Many causes of insufficient

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expulsive strength are finally overcome. They include pregnancy, inherent weakness of the abdominal wall, asthenic conditions which include ventral and diaphragmatic weakness, malnutrition, obesity, abdominal growths, faulty exercise, organic disease of the heart, lacerations of the perineum, and constitutional diseases such as diabetes, gout, leukemia, etc. Painful affections of any kind, fissure in ano, hemorrhoids, neuritis, in which the pain is increased by pressure, lead the patient to procrastinate. Masturbation and sexual excesses may provoke both intestinal atony and insufficient expulsive force. Travel is another important factor.

In children there may be *idiopathic dilatation of the colon* with enfeebled expulsive force, at times *rectal torpor* to keep up constipation (*Hirschsprung's disease*).

Spastic constipation is due to a spasmodic contraction of the intestine over separate fecal masses, usually found in nervous patients and first described by Fleiner, in which there are functional intestinal stenoses. The peristaltic unrest of the intestinal coils is recognizable. The movements are preceded, often accompanied with colic. The sphincter muscle of the rectum is also tense. Many of these cases are due to toxic influences (tobacco, excessive use of alcohol) and often the neurasthenic character is demonstrated by the association of membranous enteritis.

Of late attention has been called to a condition in which there is claimed to be abnormal movement of the cecum (*cecum mobile*). Wilms first called attention to this condition. The leading features are constipation and pain in the right ileocecal region. The acceptance of mobile cecum as a cause of the symptoms mentioned has not yet followed, and I have seen several cases in which operative interference, in no way influenced the complaints; indeed the cecum is usually found abnormally mobile without causing any symptoms.

Schmidt does not believe that the *cecum mobile* represents a clinical entity; the normal cecum is more or less mobile. The pathologic condition which causes abnormal mobility depends upon an abnormal mesentery and changes in the walls of the cecum. There are congenital anomalies of the ileocecal mesentery, diseases of the appendix, enteroptosis, obstipation, which may cause *typhlatonia*, also known as *typhlectasia*. These cases are both medical and surgical and offer a good prognosis.

Spastic conditions may be assumed to be due to insufficient moisture and too great hardness of the feces; old adhesions should always be considered possible as should other and graver lesions. We are fully convinced that the majority of constipations will yield after the correction of their removable causes, though often exceedingly rebellious. The individual case, in order to make the prognosis good and to prevent relapse, will demand thorough study and the greater success will always follow natural methods of treatment. *Constipation may be considered a bad habit when not due to organic disease of which the patient can be*

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relieved; the condition is never dangerous but it often makes the victim wretched and unhappy, handicaps him physically and mentally and often keeps up a continuous autosuggestion which tends to exaggerate the importance of the symptom enormously. The habitual use of cathartics never cures constipation.

Reference

Schmidt. Zur Frage d. Coecum Mobile. Bruns Beitr. z. klin. Chir., 1913, Bd. lxxxiii, p. 639–43.

7. Intestinal Obstruction

(*Ileus*)

While intestinal obstruction—a condition in which the intestinal content cannot be forced beyond an existing narrowing, usually mechanical, and of organic origin—is a surgical affection, it is almost invariably presented to the physician first for diagnosis.

Obstruction may be (a) partial or (b) complete. In all, x-ray examination may prove of inestimable diagnostic and prognostic value.

(*a*) *Partial Obstruction*

When partial obstruction causes but moderate stenosis (narrowing of the lumen of the intestine), the symptoms do not threaten life, constipation is prominent, persistent, and is only temporarily overcome with considerable difficulty until the prime cause is removed. There are a variety of causes of partial intestinal obstruction; some of these may never lead to complete occlusion, others may.

During the early days or months of grave intestinal disease, as *carcinoma* or *extra-intestinal pressure*, there may be only partial obstruction which as the disease progresses may lead to increasing obstruction and final occlusion. Most growths do not lead to complete intestinal obstruction.

The symptoms produced by partial intestinal obstruction depend much upon its location, cause, and the degree of constriction. It may be assumed that any narrowing of the small intestine is more likely to produce serious and threatening symptoms than is stricture of the large intestine. It is not at all uncommon to find intestinal lesions post mortem, with narrowing of the small intestine distant from the pylorus or ileocecal valve, without having caused symptoms during life. This would hardly be possible with obstruction within the duodenum or at the ileocecal valve. The partial narrowing of the large intestine at any point above the sigmoid flexure may be present, even due to malignant disease without symptoms and without threatening life during long periods (See Intestinal Cancer).

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Partial obstruction may be due to removable pressure—such as *pelvic growths* or *tumors elsewhere in the abdomen*—which may by pressure, adhesions or transitory causes narrow the intestinal lumen. The most frequent cause of partial as well as complete obstruction to the emptying of the intestines is *fecal accumulation* (40 per cent), which may follow obstipation, or *adynamia* (enfeebled intestinal peristalsis) from a variety of causes. *Gall-stones* within the intestines or by adhesions of the gall-bladder may cause incomplete obstruction.

Chronic adynamic partial obstruction may be an expression of general enfeeblement; it may be an accompaniment of central disease of the nervous system (tabes dorsalis, brain tumor, chronic meningitis, cerebral apoplexy, or other serious organic lesion). *Chronic morphinism* has in two of my cases caused fatal adynamia. *Following abdominal surgical operations,* intestinal obstruction due to acute adynamia is a serious and at times fatal combination. In such cases all of the symptoms of complete and organic obstruction may precede death. The prognosis of these adynamic cases following abdominal operation is grave. Most partial intestinal obstructions are amenable to treatment; life is not threatened, as a rule. The organic causes are purely surgical and demand radical treatment, for most of them are progressive. *Large fecal accumulations and most gall-stone obstructions within the intestines yield without radical surgical treatment* (See also later paragraphs). *Partial intestinal obstruction may exist with continuance of unsatisfactory, at times, frequent movements;* this is an important diagnostic as well as prognostic fact.

(*b*) *Complete Intestinal Obstruction*

The majority of all organic obstructions are found in the male (65 to 75 per cent) and almost one-half between the ages of 15 and 30. Between 85 and 95 per cent are in the small intestine, and as Fitz, Treves, Leichtenstein, Wiggins and others have demonstrated, two-thirds are in the ileocecal region and four-fifths in the lower abdominal regions. The various forms of intestinal obstruction are found at different ages; strangulation by bands is most frequent in advanced life and with the preceding history of peritonitis. Hernial obstruction does not often happen early in life. Intussusception or invagination is a complicaton of early childhood.

Complete intestinal obstruction is always a life-threatening condition. It demands immediate diagnosis and prompt radical treatment in almost all cases. This is true of all cases within the small intestines which arise suddenly; the gradually increasing obstructions and final complete occlusion are less malignant, but they too when located in the small intestines offer the same doleful prognosis, though the septic condition may be less virulent. *Complete obstruction of the large intestine at*

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the sigmoid may exist during weeks without causing the symptoms which promptly follow occlusion of the small intestine. Enormous dilatation of the large intestine above the stricture and surprising tolerance has characterized some of my cases.

Sepsis, peritonitis, and *final cardiac toxemia are the leading dangers of complete intestinal obstruction.*

Complete intestinal obstruction may be *acute, without preceding symptoms.* There is no warning, but suddenly the *"acute abdomen"* is developed with associated subjective and objective features at once suggestive of a grave intra-abdominal (intestinal) lesion. *Acute obstruction may suddenly develop in cases in which during a variable period there have been evidences of chronic partial obstruction;* and finally *chronic intestinal partial obstruction may gradually increase stenosis until it becomes complete. The features of complete occlusion which influence prognosis unfavorably are* suddenness of onset, shock, prompt peritonitis, profound sepsis, fecal vomiting with increasing abdominal distension, strangury, pinched and characteristic facies, cold extremities with cyanosis, and rapid small and thready pulse with hypotension after a short initial period of rise of blood pressure.

Hiccough is an exhausting symptom and is not relieved while the obstruction continues. *Indicanuria* is always present when the small intestine is obstructed, often with constriction of the large gut. *Albuminuria* is not constant but is unfavorable when present with casts. Complete intestinal obstruction may be due to:

(I) Strangulation by bands or adhesions and incarceration (hernia)
(II) Volvulus
(III) Intussusception
(IV) Stricture
(V) Tumors or foreign bodies in the bowel
(VI) Extra-intestinal pressure (from tumors, etc.)
(VII) Fecal accumulation.

In order of frequency following fecal accumulation the leading organic causes are:

1st. Strangulation by bands or adhesions and incarceration
2d. Intussusception
3d. Stricture within the intestine
4th. Extra-intestinal causes
5th. Tumors or foreign bodies in the bowel
6th. Volvulus.

The *typhlitis stercoralis* of the Germans is a condition in which there is impaction of feces in the colon with tumor formation and localized

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symptoms, with features simulating obstruction and appendicitis. The prognosis of this condition is good.

Multiple growths or tumors within the abdomen may cause symptoms simulating fecal impaction, and require cautious differentiation.

Causes of Complete Intestinal Obstruction

(1) STRANGULATION.—Strangulation or obstruction by bands and incarceration (hernia) through apertures was found in 35 per cent of 295 cases of organic obstruction by Fitz.

Treves includes

(a) Ligaments (false) following peritonitis
(b) Omental cords
(c) Meckel's diverticulum
(d) Normal structures abnormally attached (ovarian, etc.)
(e) Incarceration through slits and apertures (herniae)
(f) Isolated bands and adhesions.

(a) *False ligaments following cured peritonitis* may suddenly cause obstruction, or obstruction may be sudden after a long period of increasing symptoms, particularly *"ballooning"* or *"sausaging" of the intestine above the constriction.* The intestinal wave and distention with gurgle and collapse are easily recognized by watching the abdominal wall. *The sudden and repeated ballooning of the intestine is a symptom of great value. It is always indicative of partial obstruction and should be heeded; when it is properly interpreted in time, and treatment in operable cases is not postponed in the absence of complications, the prognosis is excellent.*

A small short or a long slender band may exist a long time without causing symptoms until a loop of intestine slips under it, and once held, the occlusion is complete. *All die unless relieved surgically.* The exceptions to this rule are so few as not to deserve consideration.

(b) *Omental cords* may cause strangulation with all of the symptoms of concealed hernia. A loop of intestine may rest in a hernial opening unobstructed, but above it a thin omental cord with adherent omentum may continue the strangulation after the hernial sac has been emptied. Unrecognized, such a complication is fatal. *Omental strings and cords with fixed omentum should always be suspected when obstruction is not otherwise explained.*

(c) *Meckel's diverticulum.*—My experience with Meckel's diverticulum proves that when it throws itself around the intestine and forms a knot, only radical treatment can save the patient. Diverticulum strangulating the gut leads to prompt collapse, usually a profound septic state, and *strangury* or scanty urine with enormous *indicanuria* in the little urine voided.

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(d) *Normal structures abnormally attached by adhesions*, organs adherent to each other, *"balling" of intestines, after repeated peritonitis*, at times adhesions to the abdominal wall, may by traction or compression cause obstruction. I have before the days of improved abdominal surgery seen tumor formation due to the agglutination described, with sudden acute or chronic partial obstruction gradually followed by complete closure. The prognosis of these conditions is not favorable when a part of general chronic peritonitis; when limited, recovery may be expected to follow surgical treatment in a large proportion of cases if instituted early.

(e) *Incarceration Through Slits and Apertures* (*Hernia*).—Isolated bands may form slits or apertures which intestines enter to be strangulated. When in the neighborhood of the appendix, appendicitis is simulated, the McBurney point is included, and procrastination will surely cause death. Experience with early operation in such cases has been favorable. I had one tabetic woman who had previously repeated gastric crises; I mistook the incarceration of a loop of the ileum into the ischiatic notch for a crisis—the symptoms were identical; when the correct diagnosis was made, the gut was found gangrenous and I lost my patient. Such a combination is exceedingly rare but with the warning and experience, the error ought not to be repeated. I have seen large and small intestines agglutinated with resulting obstruction and relief from operation.

The *herniae* belong entirely within the domain of the surgeon and rarely come to the internist. *If the majority of intestinal obstructions are to be saved, the inguinal, femoral, and umbilical openings should be suspected and examined, in spite of a negative previous history.*

(f) *Isolated Bands and Adhesions.*—I have considered these cases in connection with (e) incarceration through slits and apertures, for isolated bands may hold a loop of intestine, or adhesions with or without isolated bands may cause obstruction.

(II) Volvulus.—The gut sometimes circles or twists on itself in such a way as to narrow its lumen or completely occlude it. Fitz found 42 cases of volvulus (twists) in his 295 cases. About 70 per cent were males. One-half were sigmoidal, and in most there was an axial twist of the gut. The average age was between 30 and 40. The cecum is frequently the seat of volvulus; the ascending colon and small intestine less frequently. The prognosis of complete obstruction due to volvulus is good when operated early. If the large intestine is involved, the shock is less; the urine is not likely to be entirely suppressed and indicanuria is slight or absent.

(III) Intussusception (*Invagination*).—Intussusception is a complication of early life. The telescoping brings the six layers of the invaginated gut together (layer to layer) peritoneum to peritoneum, and if held long enough, strangulation leads to gangrene, at times to slough-

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ing and passage of the slough. In these cases it occasionally happens that nature's processes coapt the intestine and life is thus saved. In one of my cases twelve inches of gut was passed and the child lived. Osler reports one case in which 17 inches sloughed with recovery. Fitz's cases (295) were due to invagination. Lichtenstein found 52 per cent of his cases ileocecal or ileocolic, 30 per cent enteric, and 18 per cent rectal and colico-rectal.

In children invagination may be without known cause; it may complicate infections (measles), constipation, or diarrhea. Wiggins reported 103 cases in early life of which 50 per cent were between four and six months of age.

Nature's method (sloughing) and surgery, offer the only hope of saving life.

(IV) Stricture.—Stricture leading to complete occlusion and intestinal obstruction may be due to

(a) cicatrization
(b) carcinoma
(c) congenital defect.

(a) Among the causes of *stenosing cicatrization* are hernia, typhoid fever, dysentery, catarrhal ulcers, syphilis, and tuberculosis. In all of these there is a characteristic previous history of chronicity with long periods of gradually increasing symptoms (ballooning and collapse of intestine after gurgling), and when these symptoms are unheeded complete obstruction may follow.

(b) *Carcinoma and other neoplasms* are not often causes of complete obstruction because their favorite seat is in the large intestine, in the sigmoid flexure, or descending colon. When there are *annular constrictions, benign or malignant, near the ileocecal valve* they may cause complete obstruction. Cancerous infiltration of the ileocecal valve and appendix are proved to be increasingly frequent as removed specimens are being microscopically examined. When carcinoma or other neoplasm causes obstruction, surgery must be invoked. The diagnosis can, in almost all cases, be made with sufficient accuracy to justify exploration long before occlusion.

(c) *Congenital defects* are usually found in the rectum (imperforate anus or union of the pylorus and duodenum has failed). Almost all of these infants die.

(V) Tumors or Foreign Bodies in the Bowel.—Among the tumors of sufficient size to cause obstruction are polypi, fibroma, lipoma, sarcoma and carcinoma. The foreign bodies are *gall-stones, indigestible food, foreign substances swallowed* (glass, metal and a large variety of material) and *enteritis*. When *gall-stones* are of sufficient size to obstruct the intestine, they gain entrance after adhesive and localized peritonitis

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has been protective during the process of ulceration. The vagaries of gall-stones are many and Courvoisier and Elsner have reported interesting experiences which bear on this subject. The majority of large gall-stone masses which obstruct the intestine pass per rectum. Obstruction may, with gall-stones, continue during many days and yet recovery may follow. There is danger of subsequent perforation and peritonitis, but that is comparatively small. I have never been forced to resort to surgery after the stone has entered the intestine, though extra-intestinal adhesions of the gall-bladder filled with gall-stones causing obstruction almost always in the presence of threatening symptoms demands radical treatment.

Enteroliths may occasionally demand surgery to save life. Obstruction due to foreign bodies offers a favorable forecast; those dependent upon the tumors above mentioned when non-malignant, are favorable for surgical treatment. The malignant growths within the intestine when sufficiently advanced to cause obstruction are likely to have metastases and adhesions which darken the outlook.

In 44 of Fitz's cases of obstruction due to foreign bodies 23 were gall-stones, 19 were fecal masses, and 2 were enteroliths.

(VI) Extra-intestinal Pressure (Tumors, etc.).—Pelvic growths, tumors of the uterus and ovaries, pelvic abscess, retroperitoneal growths, large malignant masses connected with one or more of the abdominal organs—kidney, spleen, liver and suprarenal tissue (hypernephroma), tuberculous masses and associated adhesions—may each by pressure or traction cause obstruction. The prognosis must depend upon the operability and the complications of the individual case.

(VII). Fecal Accumulations.—We have in several of the previous paragraphs mentioned fecal accumulation as a cause of incomplete and complete obstruction, in all of which when uncomplicated, the prognosis is good. We once more call attention to *adynamic* or *paralytic ileus when neglected with fecal accumulation, in which the prognosis is always serious.* With *infarct involving the mesenterics and the abdominal wall* as a cause of adynamic obstruction, the prognosis is exceedingly grave.

Whenever there is organic, complete, acute, intestinal obstruction, the life of the patient depends upon the diagnostic ability of the physician, and the full appreciation of his responsibility which must lead to immediate surgical consultation and radical surgical treatment. I offer no statistics because they are valueless, owing to the faulty classification of the included material.

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8. Dilatation of the Colon

Hall White divides dilatation of the colon into four groups, in all of which Röntgen rays may prove of great assistance:

(I) *Distention Due Entirely to Gas.*—There is no obstruction or organic lesion. It may be an accompaniment of acute infection (typhoid fever, peritonitis, tuberculous peritonitis, traumatism, or severe nervous diseases). The result of pressure may be exceedingly troublesome, in some cases causing heart and lung symptoms, and there is extreme distention of the abdomen. When with pneumonia or chronic heart disease there is dilatation of the colon and stomach, the combination is exceedingly grave, and unless relieved may cause death. (See Pneumonia, also Acute Dilatation of the Stomach.)

(II) *Distention of the Colon With Solid Matter Within It.*—This may be due to faulty diet, coarse food, hard fecal matter, hair and other foreign substances. In the insane the swallowing of foreign bodies is a frequent cause of dilated colon; enormous gall-stone masses which have ulcerated through the intestinal wall may prove causative.

Excess of *lime phosphate* in the stool, *insufficient water, typhilitis stercoralis,* are among the causes.

Treatment and careful attention to the diet, watching the patient, thus preventing the swallowing of foreign bodies usually overcome the condition.

(III) *Organic stricture, or compression of the large intestine beyond the dilatation,* leads to hypertrophy of the muscularis when chronic and secondary changes (catarrhal colitis, ulceration, etc.) follow. The prognosis of these cases depends entirely upon the ability of the surgeon to remove the cause.

(IV) *Hirschsprung's disease, or idiopathic dilatation of the colon* —a congenital defect—is also mentioned in this section in connection with constipation (Section V, G. 6, Constipation). The dilatation, if the children live, is marked and nearly fills the abdomen. The dilatation is often progressive. There is great danger from *tetany;* obstipation is severe. The children are otherwise imperfectly developed and often show *infantilism. Acute intestinal obstruction* is a fatal complication in occasional cases, and is the most serious complication. I have occasionally met idiopathic dilatation of the colon in the adult, usually between

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25 and 30, without known cause, exceedingly rebellious to treatment with neurasthenic symptoms and cardiac neuroses. Life was not threatened. Crozer Griffith reported 24 cases from medical literature of idiopathic colon dilatation. Osler reported a case of a boy aged 10 years with enormously distended abdomen in which there was diarrhea, vomiting, and visible intestinal peristalsis. Medical and mechanical treatment were of no avail. When the abdomen was opened, no stricture was found; "the sigmoid was 18 inches in circumference, the cecum was half this size, and the bowel progressively increased in size from the cecum to the sigmoid which was folded on itself, but not so as to cause any obstruction." An artificial anus was made. There was improvement; he gained in weight; he lost his tympany but the artificial opening was never closed. But few of the congenital cases reach adult life; Kredel believes if they do, they may reach old age. I am fully satisfied that idiopathic dilatations of the colon occurs in the adult without congenital anomaly, and when it does, unless great caution in diet and exercise is practiced, it remains a chronic and annoying condition, uninfluenced by medicine but with many subjective and positive objective manifestations. Surgery offers hope of relief.

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9. Diverticulum of the Intestine

Diverticulum—a circumscribed dilatation of the intestine—may be either *congenital* or *acquired.* Aschoff classifies diverticulum as either *true* or *false.* The *false diverticulum* is characterized by coves in the intestinal wall in which the hollow opens into the muscularis and causes prolapse of the mucosa. The *true diverticulum* is characterized by a localized excavation of a part of the intestinal wall in which the mucosa is included. The one (false) is a mural, the other (true) is a diverticulum of the mucous membrane. The false is included between the mucosa and peritoneal covering of the gut. The *true diverticulum* is usually congenital. The intestinal surface has the appearance of partial perforation and the coves are most abundant and usual at the sigmoid flexure.

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The appendix may be involved, and unquestionably appendicular diverticulum is a cause of appendicitis.

Diverticulum may be *single* or *multiple.* The acquired diverticula are found in advanced life.

Diverticula may lead to obstipation, pocketing, inflammatory conditions (*diverticulitis* and *perisigmoiditis*), giving rise to serious symptoms. *Intestinal obstruction* may be caused by Meckel's diverticulum (See Intestinal Obstruction), or the smaller multiple or single diverticula may lead to stricture with consecutive dilatation, gangrene, ulceration, perforation, fistula formation (vesico-colic fistula) and distant suppuration, also thrombosis (phlebitis). In elderly subjects carcinoma is simulated. A surprisingly large number of physicians have recently suffered from the disease and have been successfully operated (resection). The results at the Mayo and other clinics where a large number of cases have been detected, have been surprisingly satisfactory. Unfortunately the diagnosis is not usually easy. Where there are persisting and increasing symptoms the condition should at least be suspected; Röntgen rays should be used to assist in diagnosis. As a rule, sufficient time for radical treatment precedes the graver complications.

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10. Intestinal Cancer and Other Growths

In connection with stricture, intestinal obstruction, dilatation, and other organic diseases of the intestinal wall I have repeatedly called attention to intestinal carcinoma in this work.

New growths may be either in the intestinal wall, or malignant nodules (good-sized masses) may by pressure (extra-intestinal) be the cause of symptoms. *For prognosis, the rule may be accepted that unless localized at the ileocecal valve, within the duodenum, at the sigmoid flexure, in the rectum low down, or at a point the function of which approximates a sphincter action, the subjective symptoms of the disease may be entirely absent during periods of sufficient length to give ample time for progression, infiltration, and even metastasis before the diagnosis is possible. When there are evidences of cancer in obstruction or in changed stools early, the diagnosis is made and the chances of the patient are consequently improved.*

The intestines, both large and small, are tolerant of malignant and non-malignant infiltration during relatively long periods; only increasing obstruction, characteristic stools (blood and mucus), x-ray pictures, and

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progressive weakness make the diagnostician suspicious. When the disease has advanced sufficiently to cause glandular invasion, near and distant, the chances of rescue are lost. There is no malignant disease which offers such surprises as cancer of the intestines. I have seen physicians with advanced sigmoid and rectal cancer who continued practice until the growth was so far advanced as to be inoperable without having created a suspicion of its presence.

Suddenly arising symptoms of intestinal flatulence and indigestion, more or less abdominal discomfort, increasing constipation and blood-streaked stools or mucus in the stools of patients at or beyond middle life, should create a strong suspicion of possible cancer and should lead to the necessary physical examination and x-ray picture to clear the horizon. I have seen brilliant results follow early diagnosis and prompt surgical treatment.

Cachexia and *profound blood changes* are not likely to be early manifestations; metastasis to the spine may precede the local symptoms. We have in suspicious cases gained considerable assistance from watching the abdominal wall for peristaltic unrest—gurgling after ballooning of the intestines. This is always suspicious. Most intestinal carcinomata are "adenocarcinomatous"; the scirrhus and encephaloid are relatively rare.

Over 95 per cent of my cases have been primary, and the rectum and sigmoid have been their most frequent seat (over 95 per cent). The statistics furnished by Brill of 3,563 cases of intestinal cancer (probably including sarcoma) showed 89, or 2.5 per cent, in the small intestine. Rolleston collected 54 cases of primary cancer of the duodenum and 19 of the ileum jejunum. My material demonstrates the further fact that over 90 per cent of cases presented with palpable masses. It is the exception to find a case of rectal or ileocecal cancer in practice before careful examination at least creates the suspicion of its presence. The late diagnosis is the discouraging feature.

Chronic cases with progressive ulceration may lead to *perforation* and *adhesions as well as multiple glandular (metastatic and distant) infiltration.* The metastases to the liver and peritoneum, particularly the former, may cause symptoms in some cases which overshadow those of the primary growth.

I have never seen a case of *rectal cancer* in a child; Matthes reports its possibility. Most cases have been in male adults in middle life. My results with rectal carcinomata surgically treated immediately after recognition have been most encouraging. I have patients living who were operated over 14 years ago. Cases of rectal cancer unoperated rarely live beyond the second year. My results have been encouraging after the early diagnosis of cancer of the ascending colon and ileocecal valve following resection. *No case of cancer of the small or large intestine recovers without surgical intervention.*

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My experience with *sarcoma of the intestine is limited.* I gather from it and the study of its literature that it is a rare condition; Libman has collected 15 cases of primary sarcoma. It may cause stenosis; the growth is primary and, in most cases, causes death in less than 12 months after its detection. Skin metastases are relatively frequent. *With stomach sarcoma, secondary intestinal masses have been found.*

Polypoid growths are benign and offer a good prognosis. Their favorite seat is in the rectum; they are also found in the duodenum. The location of these, naturally influences the symptoms and prognosis. There are a few recorded cases of duodenal obstruction from innocent growths (myxofibromatous polyps).

Myoma, fibroma, and *fibromyomata* may cause intussusception.

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H. Diseases of the Appendix

1. Appendicitis

(Inflammation of the Vermiform Appendix, Typhlitis, Paratyphlitis, Perityphlitis)

One of the most encouraging messages which this work has to offer is that *acute appendicitis, recognized during the early hours of its existence, in the absence of complications, immediately treated surgically, offers a favorable forecast in all cases.*

"The fate of the patient, the victim of an abdominal emergency, depends almost entirely upon the skill and promptitude of his doctor, and any special surgical skill has very little to do with his recovery" (Morrison).

I mention these facts at the very outset of the consideration of this subject for there are still those who, because of their doubt, are sacrificing valuable life.

History.—It is not within the province of this work to go into the history of appendicitis. The most complete and authentic data are offered by Kelly in his monumental work on appendicitis and his paper dealing on this subject. It is strange that the graphic description of the

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disease as we see it today published by Addison and Bright * in the first and only volume of their incomplete practice had received no attention. It was overlooked and it became the privilege of the American physician, Fitz, and our surgeons, Willard Parker, Hall, Sands, Weir, Bull and others, to demonstrate the surgical nature of the disease, its dangers, the fact that it was the most important of all the acute abdominal disorders, that it was the most frequent cause of what had formerly been considered "idiopathic peritonitis," and that it demanded early surgical relief that the mortality might be entirely effaced as above suggested in uncomplicated cases.

Special Considerations.—Appendicitis is a disease characterized by infection and inflammation of the appendix, deep changes in the substance of the organ with tendency to gangrene, leading to perforation and early peritonitis in the more acute cases. Beginning with the demonstration of Chauveau, who in 1882 proved that the injection of microorganisms into the peritoneal cavity might cause peritonitis, until the present day, with a growing literature to corroborate the theory of the infectious nature of appendicitis, we have learned that not one but any one of many microörganisms may be responsible for the disease. The most frequent is the *Bacillus coli communis*. *Streptococci* are at times

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* Six pages are devoted to a classic consideration of "Inflammation of the cecum and appendix vermiformis." The clinical history is clear; no work of today presents morbid appearances more graphically:

"From numerous dissections it is proved that the fecal abscess thus formed in the right iliac region arises, in a large majority of cases, from disease set up in the appendix ceci. It is found that this organ is very subject to inflammation, to ulceration, and even to gangrene, and moreover, that it is occasionally thickened and ulcerated from tuberculous deposits if the peculiar diathesis favors the change. So that this little wormlike body is often detected in the midst of the abscess, with a perforation at its extremity, or by ulceration higher up in its parietes. A considerable portion of it, nearly or entirely separated, is found in a disorganized condition amongst the pus and feces which fill the abscess. In other cases the appendix is truncated within a short distance of its origin from the cecum. In a small number of instances the cecum itself is found inflamed and ulcerated and extensively implicated in the abscess, in a way which shows that the appendix had little to do with the disease."

"Our prognosis will depend very much on the general health of the individual, and the time of life; and if both be favorable, the disease, though always of a most doubtful and dangerous character, will often slowly yield to cautious treatment. In the individual case the more favorable indications will be found in the mildness of the general symptoms and the absence of peritoneal inflammation; whereas if the contrary should be the case the abdominal tenderness becomes extreme, the prostration great, and sickness, purging, and hiccup supervene. Our hopes of recovery will of course diminish; and whatever fecal abscess has established itself, we are certain that the patient has to undergo a tedious process in which the strength may gradually give way or many casualties may arise to give a more sudden unfavorable turn to the disease."

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found without other germs or with them. The other germs are the *Bacillus lactis aërogenes,* the *Bacillus capsulatus aërogenes* the *Bacillus pyocyaneus,* the *Pfeiffer influenza bacillus,* the *bacillus of Friedländer and Fraenkel.* Stengel contends that most cases "represent a mixed infection, the most important organisms being the *Bacillus coli communis,* the *Streptococcus pyogenes,* and the *anaërobic forms.*" All are agreed that *the milder cases, with limited peritonitis and favorable symptoms are associated with colon infection; the more severe are of streptococcus and anaërobic origin.*

The absence of muscular fibers which make it impossible for the appendix to expel infectious material, fecal, or other bodies, once they gain entrance, adds to the dangers of infection and consequent progression of destructive changes. The greatest pathologic factor in appendicitis is its obstruction, either from fecal concretions, other foreign bodies, or organic change (stricture, inflammation, ulceration).

Twenty-four per cent of all cases show occlusion of the lumen. Treves found fecal concretions in 30 per cent of his cases; Deaver in 16 per cent. In 146 *adult* cases there were 63 with fecal concretions, 9 foreign bodies, in 74 nothing positive could be found. In *children,* in 49 cases, 27 showed fecal concretions, 3 foreign bodies, and 29 failed to reveal a cause. Toft in 300 examinations found evidences of appendicitis in one-third of all subjects. But few go through life without either insignificant and unrecognized catarrhal inflammation or the fully developed disease.

The irregular and anomalous course of the disease is characteristic, and often misleads patient and attendant. If the clinical histories of many cases are carefully compared, it will be found that while all have some symptoms which are alike and almost always present, there are features in the individual cases which stand out in bold relief upon which the unguarded diagnostician places undue importance, losing valuable time before reaching a correct conclusion.

The abnormal position of the appendix in many cases is responsible for anomalous symptoms, both subjective and objective. Kraussold has demonstrated the changed relations of the appendix and cecum in these cases, and it is easy to understand how the physical signs may differ from those of the majority of cases in which the location and origin of the appendix does not approach the normal. This fact is of enormous diagnostic and prognostic value, for because of it irregular and unusual subjective and objective symptoms are often incorrectly interpreted.

The inexperienced should be warned against concluding that in the absence of the *"McBurney point"* in its usual location appendicitis may be excluded, its presence is not always pathognomonic of appendicitis. The appendix may arise from either side of the cecum, it may be a little anterior or posterior, a little nearer the head of the colon than normal;

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it may arise from the very edge of the cecum, higher than normal; indeed I have found it so high as to lead to the conclusion that an appendicular abscess was the distended gall-bladder. Kelly and Hurdon report the appendix placed horizontally toward the promontory, or pointing laterally in 32 per cent; oblique toward the spleen in 10 per cent; ascending in 34 per cent; descending in 24 per cent.

Another cause of misleading and anomalous distribution of pains and other features are the *reflex symptoms* which lead to distant symptoms in both acute and chronic cases during dangerously long periods. Thus *I have seen renal colic simulated by appendicitis during the first twenty-four hours of its existence, and only the dependence upon the partially developed physical signs of the disease with a suggestive leukocytosis saved the patients' lives*—the appendix was so placed as to occlude temporarily the right ureter.

The radiation and localization of all pains from the epigastrium or hypochondriac regions may prove misleading and expensive. Left-sided pain with anomalous location of the appendix demands cautious examination and consideration of separate symptoms and blood counts.

The frequency of appendicitis fully appreciated, will often lead to safe conclusions in the absence of typical pictures, but with a few symptoms which are suggestive.

The *age* of the patient is of great prognostic significance. Treves' statistics bearing on the incidence of the disease shows it most frequent between the tenth and twentieth year. He offers the following, showing the percentages:

5 to 10	10.8	per cent.
10 to 20	40.7	" "
20 to 30	29.0	" "
30 to 40	11.5	" "
40 to 50	4.6	" "
50 and over	3.4	" "

Children between 5 and 10 years of age in unoperated cases show a high mortality. In 1906 in Prussia, the mortality in the first fifteen years of life in one thousand cases was 14 to 16 per cent; from 15 to 30, 6 to 7 per cent. Heubner had a mortality of 15 per cent; only 3 were operated. Neuberg claimed the mortality following operations about 23.4 per cent, unquestionably due to late operation. Riedel reported a mortality of 16.4 per cent in 310 children operated. He reduced the mortality in the adult during 21 months to 2.9 per cent, while the death rate among the children during the same period was 13 per cent. In Germany there has been great objection by parents to the early operation of children so that the statistics compare unfavorably with our own.

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The mortality in the adult during the active period of life has been reduced in America to an almost negligible figure when operation is early. In patients beyond middle or in advanced life the mortality rises with increasing age. The character of the lesion is of paramount prognostic value.

Catarrhal Appendicitis

Unquestionably the majority of catarrhal appendicitides escape the physician, because they are so insignificant as to demand no treatment and the patient may remain without subjective or objective symptoms. Simple catarrhal appendicitis may remain subacute, give rise to dyspeptic symptoms without recognizable fever or local physical signs, and recover fully. Recurrence is likely. There are a large number of mild, acute cases which make early diagnosis possible in which there are no evidences of localized peritonitis, no rigidity, no changed percussion note, insignificant tenderness, but slight elevation of temperature and moderate leukocytosis, pulse practically normal, in which after from two to four days all subjective symptoms are overcome. The large proportion of cases which demand our close study are those of catarrhal character in which the diagnosis is possible and positive before the end of twenty-four to forty-eight hours, in which there is slight rigidity, some fever, at times slight chill, and slightly accelerated pulse. There may or may not be vomiting. Many of these cases do offer a good prognosis without operation. Many of these, considered favorable, suddenly change their features and present evidences of extension, increased rigidity, increasing distension, obstipation, with or without rise of temperature. Most of these vomit more or less. These cases are serious; they may perforate. Ulceration without perforation may cause peritonitis—toxemia—overpowering and fatal.

There are no criteria which make it possible for the clinician to tell whether the simple catarrhal type of the disease is to remain so, whether an ulcer which results from the infection is to perforate or cause local or diffuse peritonitis, whether there will finally be abscess formation or other complication. The catarrhal form of the disease with physical signs sufficient to make the diagnosis positive with leukocytosis and rigidity (it matters little what other symptoms are present) is positively a surgical disease, the prognosis of which is enormously improved by early operation. Spreading symptoms after a period including the clinical picture described in the preceding paragraph are evidence of increasing infection from which the majority *die* unless saved by radical treatment.

Catarrhal cases may present with increased pain and fever, when a short period of relief may follow. The temperature in such cases may fall; the pulse may or may not show improvement—usually it does not vary much. Under such conditions I have frequently met patients and

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physicians who opposed operation. Such relief of pain is insignificant if the local physical signs (rigidity particularly, and slight dullness) persist. The chances are that there is either perforation or deep ulceration which will ultimately perforate, and within from twelve to twenty-four hours increasing distension and rapid heart will indicate the presence of peritonitis. In one case seen in consultation in which there were the initial symptoms of catarrhal appendicitis, later exacerbation of symptoms, vomiting and localized rigidity, there was *fall of temperature;* the rigidity remained though the pulse was slower; leukocytosis continued. I insisted on operation, and found the appendix with three perforations. Fortunately protective peritonitis prevented diffuse inflammation and the boy (aet. 20) recovered. *Failure to interpret the meaning of the apparent improvement of subjective symptoms may lead the attendant and patient to false conclusions with disastrous results.*

A large number of mild or catarrhal cases recover from the acute symptoms, but slight tenderness remains and dyspeptic symptoms are likely to develop. Some of these show *hyperacidity* and with slight acute exacerbations of pain, no marked increase of local physical signs or fever, they gradually merge into chronic appendicitis.

Not a few during the first twenty-four hours are apparently mild catarrhal cases, when in truth they have been ulcerative and gangrenous from the beginning. These are often *fulminating,* and unless promptly relieved by operation they are almost always fatal.

In the process of repair and "cure," the possibility of thickening of the organ, constriction, distortion, dilatation below the occlusion and late abscess formation, as well as suddenly arising localized or diffuse peritonitis are to be considered. In some cases the thickened appendix remains tender, may never cause acute symptoms, but is sufficient to limit the efficiency of the patient.

Purpuric Appendicitis

Occasionally there are cases in which the earliest evidence of purpura hemorrhagica is hemorrhage into the substance of the appendix causing all of the symptoms of acute appendicitis. I have had two such experiences; in both operation proved the hemorrhagic nature of the disease and hemorrhages from various sources (mucous membranes and into the skin) followed. Both recovered.

Fibrinoplastic Appendicitis

The appendix infected, the fibrinoplastic deposit may be prominent. The exudate may not limit itself to the appendix but there may also be either localized, or moderately diffuse, or general fibrinous peritonitis. Catarrhal inflammation, primarily with or without ulcer or necrosis, may

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cause plastic exudate. It may happen that in such cases the peritoneum is protected by localized fibrinous deposit which organizes later, and leaves a thickened appendix with or without adhesions. These are among the *chronic appendicitides*, which when they cause subjective symptoms are never relieved permanently save by operation.

The prognosis of uncomplicated fibrinoplastic appendicitis for life is favorable without operation; the tendency to relapse is great, and a large number of chronic cases are easily traced by the pathologic lesions to this form of the disease.

Fibrinoplastic appendicitis may finally be complicated by ulceration of the mucosa, diffuse peritonitis or abscess formation, due to perforation.

Perforative Appendicitis

Perforation is the result of infection and necrosis; it is at once the most serious of all appendicular lesions associated with its acute inflammation. Catarrhal ulcers, as suggested in the preceding paragraphs, may perforate or the infection may cause early deep and destructive changes leading to death of tissue at one or more points.

Three per cent of *typhoid appendix ulcers* perforate. Perforative peritonitis unoperated and advanced beyond the first twenty-four hours, offers an unfavorable forecast.

The perforation, when preceded by nature's protective exudate (protective peritonitis) may not open into the free peritoneum but into a sac; an abscess is likely to form, which may or may not perforate in one of many organs.

The sac may perforate into the peritoneal cavity with resulting general septic peritonitis. Almost all of these cases when advanced to this stage die. There are in most cases of perforative peritonitis which are not fulminating, "factors of safety" which seek to prevent extension by protective and localized peritonitis during the early hours of the process.

The gravest of all cases are those which without tumor or protective exudate; adhesions, or localized peritonitis, open directly into the cavity of the peritoneum, causing diffuse acute peritonitis. These patients show early the overpowering and deadly influence of toxemia, which includes the symptoms whose prognostic significance will be separately considered.

General diffuse peritonitis due to perforation is separately considered (See Acute Diffuse Peritonitis); it offers, when due to perforation, only the gravest outlook.

General diffuse peritonitis may be caused by infection from deep ulceration of the appendix without perforation. The anatomic location of the appendix is an important factor in determining the point of perforation, the location of the appendicular abscess and the nature and extent of the resulting peritonitis.

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Rupture into a hollow viscus is naturally much more favorable than is perforation into the free abdomen.

Retroperitoneal abscesses are within easy reach, and offer a good prognosis; these may rupture into the ileum, cecum, duodenum, diaphragm, colon, bladder, acetabulum, externally, through sinuses, or directly into the peritoneal cavity.

The ultimate fate of *pus accumulation* is of great importance. It is difficult to give a forecast. The presence of pus remains a menace; it may cause sudden diffuse peritonitis by perforation; it may open in any one of the directions above mentioned. While there will always be cases which empty without threatening life, the large majority left untreated lead either to subacute or chronic pyemia or to fatal peritonitis. The prognosis of appendicitis has been enormously improved by the prompt evacuation of the abscess cavity. Other secondary complications are thus prevented, such as liver and kidney abscess, pylephlebitis, occasionally meningitis and other grave organic changes.

The presence of previous disease (particularly *chronic nephritis* and *heart lesions*) always handicaps the patient. Chronic nephritis with appendicitis invites infection and deep-seated ulceration, perforation, and rapidly spreading peritonitis. The same is true of *diabetes mellitus and other metabolic diseases.*

Tonsillar streptococcus infection as well as the *Streptococcus rheumaticus of Poynton and Paine* may precede appendicitis, which may then be considered *metastatic.* Jores and Aschoff have also reported *metastatic appendicitis with scarlet fever.* The latter cases are always serious because of the primary sepsis.

Influencing Factors

Leukocytosis.—*Increase of polymorphonuclear leukocytes* is practically constant. There are exceptions, but they are so few as to demand but little consideration. My average count at the first visit is rarely below 12,000, usually nearer 15,000. Counts above 15,000 early, are indicative of pus accumulation. Fully developed appendicitis shows an average of 85 to 90 per cent of polynuclear leukocytes and white counts between 20,000 and 25,000. Symptoms of increasing peritonitis with increase of leukocytosis are suggestive of perforation. The white count is of much greater diagnostic than prognostic value.

Heart.—*The condition of the heart and the study of the pulse* offer data for prognosis of the greatest value.

In *fulminating cases,* the sudden toxemia finds expression in marked *cardiac asthenia.* It is always unfavorable to find children with rapid pulse and erratic systolic action during the early hours of the disease. In adults, grave local lesions may be associated with a tense, not of neces-

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sity rapid pulse, and slight rise of temperature during the first hours; but with advancing disease (if perforative), the pulse grows progressively more rapid and weaker, while the blood pressure falls. The pulse may not be materially accelerated; indeed we have found it surprisingly slow, in the presence of perforation or ulceration without perforation. In such rare cases the diagnosis and prognosis must depend upon the physical signs and other subjective symptoms.

Perforative peritonitis may in its early stage, as I have already suggested, show an unchanged pulse, a decided drop of temperature and relief of pain. The recognition of such possibility means much to the patient; failure seals his fate within twelve to twenty-four hours.

The rule may be accepted that in the adult a *rapid pulse from the beginning is unfavorable and indicates profound toxemia and deep tissue changes.* Rapid pulse with septic symptoms in patients with good resistance does not argue against the possibility of recovery. Such cases frequently recover after operation. Unchanged and rapid pulse after operation (within 24 to 36 hours) considered alone or with other symptoms, is evidence of a severe condition.

Improved systolic force within the first twenty-four hours following operation is always reassuring. The pulse is slower and fuller and usually the general appearance of the patient and other symptoms show decided change also.

Intermittent heart, arising at any time during the course of the disease, must be considered among the grave symptoms if the frequency is materially increased and the heart sounds are feeble.

Sudden heart dilatation is possible and should be anticipated by the attendant in cases where the previous history leads to the suspicion of a diseased myocardium. *Thrombosis of the pulmonary artery or one of its branches* may cause sudden death.

Temperature.—*Initial chill* is not the rule; "chilly sensations" are frequent with rise of temperature during the first twenty-four hours. The temperature during the first twenty-four hours does not offer anything upon which the prognosis of the individual case can be based. The rise of temperature may be so insignificant in serious cases as to deceive the attendant and lead away from the correct diagnosis. Taken alone, temperature therefore is of little value for our purposes. There are those who hold that there is always rise of temperature early; this is probably true, but failure to detect it with other suggestive symptoms must not overthrow the diagnosis.

Gradual rise of temperature in spite of surgical treatment and rapid heart, with or without change in the local symptoms, justify only an uncertain prognosis not necessarily unfavorable; the general picture of the case as seen after giving all of the symptoms their relative value will usually lead to safe conclusions.

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Repeated chills and fever after operation indicate pus accumulation and sepsis. Repeated chills, rapid pulse, jaundice or icteroid appearance, are suggestive of *pylephlebitis, thrombosis, secondary abscess of the liver, involvement of the gall-bladder or bile passages.*

The reappearance of fever after fall, following operation, is indicative of some complication which in most cases is not serious.

Vomiting.—Early persistent vomiting is characteristic of the more severe cases; when distension rapidly follows or rigidity increases, there is usually a serious underlying ulceration, perforation, or a severe type of catarrhal appendicitis. *Fecal vomiting* early, indicates perforation; fecal vomiting later attends perforative peritonitis and *adynamic intestinal paralysis.*

When vomiting is controlled by the operation and suddenly returns, it demands the thorough consideration of possible *intestinal obstruction* (either *mechanical* or *paralytic*) and makes the outlook grave. The prognosis depends on the ability of the surgeon to remove the cause. I have seen a number of fatal cases in adults operated late; there was beginning *perforative peritonitis*—death followed after two or three days of vomiting which finally became fecal, the distension increasing, hiccough was uncontrolled; these cases represent the *adynamic intestinal paresis* above mentioned.

It may be concluded that the *prognosis is always bad when vomiting does not yield promptly to surgery or medical treatment.*

Hiccough.—Early or late hiccough is always an ominous symptom. When early, it is usually associated with the fulminating type of the disease; when late, it is very likely to be a symptom of diffuse peritonitis with intestinal paresis; when it follows surgical operation, it may be due to one of several conditions (obstruction, band formation, adynamia, uremia, acidosis, diffuse and increasing peritonitis, etc.).

Obstipation.—I mean by "obstipation" obstinate constipation without positive organic obstruction of the intestine. But few cases of appendicitis are of serious moment in which the bowels are open and free. I do not remember to have lost such a case. The cases with obstipation from the beginning are very likely to include those with the deepest appendicular and peritoneal changes.

Pain.—*Severe pain with prompt distention and early rigidity is suggestive of the graver types of the disease.*

The milder forms are less painful than are the severer during the early hours, and as a rule it is possible for the patient to get into a position which makes him fairly comfortable most of the time.

The *McBurney point* is tender and present in those cases in which the origin of the appendix is normal or nearly so (about 60-70 per cent). Tenderness over an abnormally large area is indicative of peritonitis, either local or diffuse.

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Cessation of pain during a limited period following perforation is not infrequent, and is of great prognostic significance.

The *location* and *radiation of pain* offers some indication of the relative position of the appendix. Severe backache may characterize pain with abscess or appendicitis in which the origin is posterior. These cases offer a good prognosis and with pus are easily drained, without opening the peritoneal cavity. It would lead to unsafe conclusions if pain as a symptoms were depended upon for prognosis. It should not be forgotten that severe and fatal cases may begin with but few sensory symptoms.

Hyperalgesic areas (Head zones) are of diagnostic, and not of prognostic value.

Albuminuria and Indicanuria.—Most perforative and ulcerative cases in which there is toxemia show evidences of *toxic nephritis* if the urine is cautiously watched. A faint trace of albumin with free secretion is not serious. Marked reduction in quantity, albuminuria and casts (blood, hyalin, granular) is always grave. Cases in which albuminuria depends upon previous nephritis with any form of appendicitis are serious—not of necessity fatal. These cases early recognized, in the absence of heart lesions, offer a fairly good prognosis.

Sudden *strangury*, following preëxisting albuminuria whether early or late, is of grave moment.

Indicanuria is present in most cases. Its presence taken alone is of no prognostic value. Bacilluria and albuminuria *per se* are not of necessity serious.

Facies and General Appearance.—The facies with the *"acute abdomen"* are characteristic; the pinched appearance, sunken eye, anxious expression with clear mind, as a rule, are not easily forgotten. Hippocrates described the facies of acute peritonitis (facies hippocraticus). The experienced eye sees in the facies, the general appearance and position of the patient in bed, much that is either encouraging or discouraging. In no other disease are the facies more expressive. In extreme danger, the facies hippocraticus with cold extremities, congested conjunctiva, hiccough and fecal vomiting and small rapid pulse, tell of approaching death.

Physical Signs.—*Increased abdominal resistance—rigidity—is the most important physical sign of acute appendicitis.* The *clinician who appreciates the significance of rigidity early and treats his cases secundem artem will reduce his mortality to a negligible figure.* There are but few cases in which cautious examination will fail to show some increased resistance in the region of the appendix. Light *percussion* will show some dullness, and palpation in many cases makes it possible to palpate a mass of varying size. Rigidity is the more dependable of all of these signs; the one which should lead the attendants whenever present. Its presence justifies the disregard of most other symptoms. *It always means*

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something; it should never be ignored for safe prognosis and treatment.

The size of the tumor with its attending physical signs is also important. *Palpable tumor without physical signs of general peritonitis* proves pus accumulation in almost all cases. *The circumscribed tumor* is evidence of the success of nature to limit the disease, and offers an excellent prognosis. *Increasing distention, tympany,* is always suggestive of peritonitis or adynamic paresis and is usually serious. *Perforation or deep ulceration, with diffuse peritonitis is usually found.*

Effacement of liver dullness appearing suddenly, is symptomatic, but by no means pathognomic of perforation. I have met it in cases without perforation; at times after operation, or even before, in which recovery followed. As a rule, however, marked tympany with effacement of liver dullness is a combination which justifies a doleful forecast. Naturally other symptoms show the danger also.

Relapse—Recurring Appendicitis

Forty per cent of unoperated cases relapse. Some of these merge into chronic appendicitis, others after one or more relapses cause perforation; a proportion of these form abscesses, others have fulminating peritonitis, some localized peritonitis, while with the majority of perforations the dangers of acute diffuse peritonitis are faced. Some of these cases which appear to be mild during one relapse may in the next, or one of the subsequent attacks, perforate unexpectedly.

Saviaraud found that in children the mortality in the cases which followed procrastination was 32 per cent. Sahli found in 7,213 cases of which number 6,740 were not operated, recurrence followed in 4,593. Of these he claims 3,635 recovered without further recurrence.

Chronic Appendicitis

Any form of acute appendicitis which lives after the initial attack may leave remnants of the infection which finally cause persisting symptoms, or without an original acute attack, chronic appendicitis may gradually develop. Chronic appendicitis is subject to acute exacerbations of both local and distant symptoms. I have considered chronic appendicitis as a cause of dyspeptic, gastric, and gastro-intestinal symptoms in connection with a number of diseases, which the reader will find included in this section. In all chronic unexplained dyspepsias, chronic appendicitis should be suspected.

Adhesions and thickening, distortion, retained foreign bodies (fecal concretions), pus accumulation, may continue symptoms during unlimited periods. The symptoms once present with a chronic underlying change do not often yield; they do not threaten life unless there are acute exacerbations, perforation, intestinal obstruction from extensive adhesions

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or other grave complications; but the majority continue with dyspeptic symptoms, chronic constipation, pain varying in severity from time to time, often inefficiency in many directions, including mental lethargy. The prognosis of these cases when operated is excellent. A large material during the past twelve years has been without a single death following *interval operation;* most have made full and satisfactory recoveries. With extensive adhesions some symptoms may persist, but in practically all, the patients were markedly relieved.

There is danger of *intestinal obstruction* in cases in which symptoms of chronic appendicitis persist with adhesions of the ileum and at times tumor formation. Such cases demand early attention to prevent strangulation of the intestine (See Intestinal Obstruction). The symptomatology and prognostic significance of *Jackson's veil and the conditions which Lane in England and Bainbridge in this country have described under "intestinal stasis,"* and upon which the latter place great stress as producing the symptoms of many diseases, are all surgical. I am fully satisfied that the *Jackson membrane* causes persistent symptoms which may be relieved by surgical interference in individual cases, for I have had telling experiences. Adami has fully and well answered many of the contentions of Lane, to which the profession has not subscribed; there may be justification in isolated cases to assume that the conditions which Lane describes cause some symptoms, but the galaxy of diseases to which he refers in his recent publications will never be included.

Cancer of the Appendix

Cancer and carcinoid of the appendix are more frequent than is generally supposed. Rogg reports 58 in 11,000 cases of appendicitis, and reports 200 cases taken from medical literature. The microscopic examination of appendices removed by operation is showing an increasing number of cases. Most of these are found early in life—in the third decade. They may be either intramucous, submucous, or subserous (carcinoid). Their favorite seat is the tip. Some involve the entire appendix by infiltration, and in some there is a distinct history of preceding acute and final chronic appendicitis. In these cases in young subjects there are few or no metastases; the course seems to be benign, and early operation offers a good prognosis. With the valve and cecum involved, I have not had brilliant results from resection. All cases in subjects after fifty promptly recurred and died within twelve months. The growth is rapid after fifty and metastasis is the rule.

Tuberculosis of the Appendix

See Intestinal Tuberculosis, Section I.

Primary tuberculosis of the appendix is possible, but rare. *Tuber-*

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culous ulceration and appendicitis are usually secondary to similar disease of the lung, intestine, and peritoneum. The prognosis of the primary disease is not bad.*

Appendicitis and Typhoid Fever

Appendicitis is not frequent with typhoid fever. Typhoid ulcers of the appendix are relatively frequent. Rolleston found the appendix altered in 14 of 60 cases; in 5 it was swollen, in 7 ulcerated, and in 2 perforated. Fitz found in 167 typhoid perforations that 5 were situated in the appendix; Curling found 20 typhoid perforations with 2 in the appendix; Church 3 of 21; Morin 12 of 64; and Heschl reports 56, in 8 of which the appendix was perforated. Kelly finds that appendicitis with typhoid may be purely accidental—the two conditions are concurrent, or latent appendicitis is lighted into activity by typhoid fever. Appendicitis, either mild or severe, may arise during typhoid from lymphatic infection or from an appendicular typhoid ulcer. These latter cases often perforate. Typhoid fever may be followed by appendicitis, following so soon as to suggest typhoid infection of the appendix.

Naturally the prognosis is more grave with typhoid appendicitis than without such complication or when the patient has been in perfect health. Surgeons are agreed that "the symptoms to justify operation must be of a more urgent character than would be necessary in the case of a person in perfect health suddenly affected in a similar manner, as the greater gravity of an operation in the height of typhoid fever warrants the surgeon's assuming greater risks in waiting to make sure that an operation is inevitable" (Kelly). Of seven typhoid perforated appendices operated, only one recovered.

Cushing believes that the prognosis of appendicular perforation with typhoid is better than perforation of the ileum. The toxemia and typhoid lesions with added appendicitis present a complication of extreme gravity. No surgical complication will demand more judicious care. Richardson has accented the great danger of operations during typhoid fever. In the absence of perforation which demands operation, the prognosis is good without operation. This has been the experience of most clinicians and surgeons (Murphy, quoted by Kelly).

Complications

I have recently referred to the dangers of *nephritis*—usually toxic—as a complication of appendicitis and peritoneal infection. *Preceding chronic nephritis with or without uremia* is always of grave import.

* Schnitzler considers this subject fully in an able article, to which the reader is referred for further information.

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Toxemia is invited by this complication and in many of my cases the course has been surprisingly rapid and fatal.

The cardiac complications have been mentioned in considering the pulse. Preceding *myocardial disease, valvular lesions with faulty compensation* in the presence of added toxemia, often lead to *cardiac asthenia* during the early days of the disease. *Pylephlebitis* with or without pus deposits (*abscess of the liver*) is a grave complication; when extensive, death usually follows after a period of pyemic septic symptoms.

Septic phlebitis—thrombosis—may, according to location and constitutional involvement, cause grave symptoms during only a short period, or chronic phlebitis may develop and lead to weeks of invalidism. The septic type of thrombosis with marked toxemia and involvement of the sensorium is usually fatal.

Pneumonia, empyema, non-purulent pleurisy are occasional complications. The first, in severe cases, is exceedingly grave; the second during convalescence after operation usually yields to operation; the third offers the same prognosis when a late complication as when the disease is primary. In all, the resistance of the patient is paramount. *Typhoid fever* may follow appendicitis when the prognostic features are materially influenced by lack of resistance following the original disease.

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I. Diseases of the Peritoneum

1. Acute Diffuse Peritonitis

(*Inflammation of the Bowels*)

General Considerations.—Peritonitis may be either circumscribed or diffuse. It is almost always of bacterial origin and practically always secondary. *"Idiopathic peritonitis"* has fallen into oblivion. Those cases of nephritis, tonsillitis and other diseases which were closely associated by the older clinicians with unexplained peritonitides are now known to be of bacterial origin, or to have an added infection which explains the inflammation of the peritoneum.

The cases which Flexner has characterized as *primary* "are those originating apart from disease of any neighboring organ, or in other words cases due to metastasis by way of the blood or lymph stream"; hence these, too, may safely be considered secondary. *Peritonitis with rheumatic infection,* formerly considered *"rheumatic peritonitis,"* depends upon bacterial invasion, is rare, never primary, and offers a high mortality. Osler mentions acute peritonitis *"as a terminal event"* in *nephritis, gout,* and *arteriosclerosis;* 12 were found in 102 cases of acute

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peritonitis at the Johns Hopkins Hospital. My material reduces the number of such incidents far below these figures. Flexner includes among the secondary cases those infections of the peritoneum due to injury or disease of an organ in direct contact with the peritoneum. The infecting agent may enter from without the body (exogenous), or it is endogenous when it comes from within (Allchin).

Flexner's 106 cases included only 2 in which he was unable to determine the variety of the bacterial infection. *Bacterial virulence and proliferation* are invited by the inability of the peritoneum to take advantage of its "factors of safety," or normal protecting power. Thus in the presence of fluid in the cavity (injury or disease) with ascites, as in nephritis or other lesions, with perforation, and foul and other foreign matter, the protective agencies are reduced, and proliferation is invited; virulence, as suggested, is increased. These facts are sufficient to explain the rapid development of acute peritonitis following injury to the abdominal wall, the breaking of adhesions, perforations, uterine lesions, salpingitis and the many other primary diseases which promptly cause the secondary disease. In the preceding chapter I considered the association of peritonitis with appendicitis—the most frequent of all of the causes. I have also considered peritonitis as it complicates the various intestinal obstructions, including hernia and constriction due to intraintestinal lesions, with the perforation of typhoid, stomach and duodenal ulcer, also malignant ulceration and perforation, gonorrheal and puerperal infection of the genitalia, and their dependencies. It would be a work of supererogation to again dilate on each of these. The resulting peritonitis offers the same general picture; its gravity is always the same though the virulence and malignancy of the infection does influence the resistance of the individual, but with all the rule holds that it is the rare exception for a case of general peritonitis, in which the cause has not been promptly removed, to recover. *Once peritonitis is general from whatever cause, the chances of saving life are exceedingly small. Septic* (streptococcus) *peritonitis* leads to such profound toxemia as promptly to rob the patient of heart strength.

Localized and protective peritonitis is often a life saving process, for by the throwing out of plastic material and its organization it protects against general and septic peritonitis. This is often true of ulcerative intestinal diseases (appendicitis, intestinal, gastric, duodenal ulcer, and gall-bladder disease).

Subphrenic abscess is considered with ulcer of the stomach and duodenum; for its clinical study Maydl's monograph is a classic.

It may be assumed that *the sudden development of general peritonitis following perforation of a hollow viscus, without preceding protective peritonitis, is among the most serious forms—almost always fatal unless detected at once and relieved by surgical treatment* (perforative peritonitis).

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In these cases the *Streptococcus pyogenes* is usually found, the *albus* is less virulent. In children the *pneumococcus* is among the more malignant of the bacteria present (Rischbieth). The gonococcus in my experience is less virulent than the streptococcus and often leads to a subacute or chronic course. Prognosis is materially influenced by the resistance which rugged health and the normal previous conditions offer. *Young children particularly offer a bad prognosis in acute peritonitis from any cause.*

Acute Diffuse Peritonitis with Appendicitis.—With appendicitis (the usual cause) *diffuse peritonitis once developed is almost uniformly fatal.* The unfavorable features are pronounced abdominal distention, obstipation, fecal vomiting, hiccough, pinched features, reduced and albuminous indican-laden urine, small pulse, rapid heart, hippocratic facies, and cold extremities. Never have I seen but two patients recover with this symptom complex.

The Temperature.—The temperature in the midst of fully formed symptoms is not to be depended upon as a prognostic index. *Prompt collapse with subnormal temperature* in the early hours of peritonitis is only occasionally followed by a happy result. *High temperature* is unfavorable in the presence of other advancing symptoms. *Extreme restlessness and insomnia* are always unfavorable. The average duration of *fulminating or perforative appendicitis* is rarely beyond forty hours.

Treves mentions cases in which the peritoneal symptoms are less prominent than is the *typhoid condition.* These are in aged and previously reduced individuals.

Kidney and Liver.—Among the serious secondary lesions are those which involve the kidney and liver. The rapid advance to the liver through the portal circulation of toxins from the abdominal cavity and to the kidney lead to parenchymatous changes. These add factors of enormous danger.

Puerperal Peritonitis.—Puerperal peritonitis is fortunately rare when modern methods are used during labor; it is a streptococcus infection, is probably of lymphatic origin, and spreads from the uterus to the peritoneum. Continuous fever with rapid pulse is less favorable than remission with profuse sweat, following chill and fever. It is a true septicemia. The mortality is rarely below 50 per cent in developed cases.

Further Considerations.—In all forms of the disease the more favorable cases are those in which the intestinal paresis is not complete, and there are occasional movements with fair quantity of urine and a heart which is without the asthenia of extreme toxemia. When the pulse is persistently at 120 and above, the condition of the patient is threatening, whether before or after operation. The conclusions offered in considering the *blood picture* and appendicitis, are equally true of peritonitis. High leukocytic counts are not encouraging—low counts are equally unfavorable.

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Diffuse peritonitis as a rule, when it is not controlled within the first 30 hours, is fatal.

I have learned to place great reliance in prognosis on the facies of the patient. Changed facies, pinched appearance, means death. Of Treves' 70 fatal cases 14 per cent died within 36 hours, 6 per cent between 36 and 48 hours, 20 per cent between the third and fifth day, 33 per cent between the fifth and seventh day, and 27 per cent after a week.

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2. Chronic Peritonitis

After acute localized peritonitis there is organization of tissue (*productive peritonitis*) which leads to thickening and adhesions (periuterine, perigastric, perisplenic, periappendicular). In occasional cases there may be *pus accumulation* between the layers of new tissue. Such *abscesses* are naturally encapsulated and usually operable, and offer a good prognosis. These include appendicular and subphrenic as well as other abdominal abscesses.

Deforming and obliterating peritonitis or adhesive peritonitis follow in those cases of agglutination in which after acute or subacute peritonitis or the tuberculous variety, the coils of intestine or organs are so firmly united as to make separation impossible. The *peritoneum is obliterated and "deformed."* Such complications are also likely to follow extensive abdominal operations.

Periserositis (See Pick's Disease and Periserositis) may also be included among the chronic types. In these cases besides the spleen, the liver, general peritoneum and pericardium are included.

The great *dangers of localized and obliterating chronic peritonitis, are possible intestinal obstruction and chronic invalidism, due to the effect of adhesions, bands, distortions, and the changed relations of organs. In-*

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testinal obstruction due to fibrous bands and adhesions is fully considered elsewhere (See Intestinal Obstruction).

Chronic Nodular Proliferative Peritonitis.—Pathologists and clinicians are familiar with a form of productive chronic peritonitis with nodular growths of the peritoneum and thickening, which so closely resemble tubercle, as to be differentiated *intra vitam* (at the time of operation) with the greatest difficulty. Welch calls attention to such cases in his section on the pathology of peritonitis in Flint's "Practice of Medicine," also in his discussion of Nicholl's paper. Such cases are undoubtedly at times included among the tuberculous, and are favorably influenced by surgical interference. Fitz and Wood also mention such possibility. The thickening and agglutination in these cases may lead to tumor formation, either single or multiple; the viscera are covered with tense and thick peritoneum; circulatory embarrassment and ascites, at times obstruction, cause of death. I have found the productive (proliferative) peritonitis with *alcoholic cirrhosis.* In *children* I have occasionally seen chronic nodular non-tuberulous peritonitis with ascites and chronic invalidism. Some of these cases yield after operation; a few have made satisfactory recoveries without. Most of these children recover.

General Conclusions.—*Chronic peritonitis may complicate malignant and echinococcus* involvement of the peritoneum when *hemorrhagic ascites* is likely. Whether *"hemorrhagic peritonitis"* is ever primary is questionable.

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3. Tuberculous Peritonitis

See Tuberculosis, Section I.

4. New Growths of the Peritoneum

I have never in practice seen a case of primary cancer of the peritoneum. Neoplasms (malignant) of the peritoneum are practically always secondary. *Fatty deposits* (*lipoma*), *fibroma,* and *neurofibroma* are occasional benign growths which do not materially interfere with the patients' comfort as a rule, and are operable if large and troublesome.

Innocent cysts and *echinococcus* of the peritoneum offer a good prognosis (See Echinococcus Disease).

Aschoff calls attention to a diffuse *endothelial degeneration* of the peri-

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toneum which he considers primary and malignant (endothelioma). The prognosis is bad.

The *secondary carcinomata,* usually multiple and disseminated, are found with stomach, gall-bladder, bile passage, pancreatic, intestinal (rectal often), ovarian, uterine, and renal (*hypernephroma*) growths. The *mesenteric glands* are involved; *ascites* is prominent—usually bloody—and after varying periods with characteristic facies and marasmus, death follows.

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J. Diseases of the Liver

1. Jaundice

(*Icterus*)

Surcharged fluids and tissues of the body with bile coloring matter cause a yellowish coloration of the skin, mucous membranes, and conjunctivae, easily recognized and known as jaundice.

Jaundice is never a disease per se; it is always a symptom and is due to obstruction of the flow of bile, which may be either complete or incomplete, in almost all cases.

(a) *Hepatogenous jaundice is always obstructive* and is due to the resorption of bile manufactured in the liver which fails to escape from that organ, wholly or in part.

(b) *Hematogenous or hemo-hepatogenous jaundice* is due to the change of hemaglobin into hematoidin, identical with bilirubin. In these cases there is rapid destruction of large numbers of red blood corpuscles—*hemolysis, causing hemolytic jaundice; the hemoglobin is converted into bilirubin in the liver in most instances. Recent experimentation tends to prove the possibility of such conversion in the blood stream.*

(*a*) *Hepatogenous Jaundice*

(*Obstructive Jaundice*)

Causes.—The larger number of cases are due to *mechanical obstruction* in which there is reabsorption of bile which cannot escape into the intestine through the common duct. The most frequent *causes of obstructive jaundice* are (1) *catarrhal inflammation of the duodenum and common duct with consecutive closure at the opening of the ampulla of Vater* (*catarrhal jaundice*). Among the other causes of mechanical obstruc-

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tion leading to jaundice are (2) the *impaction of gall-stones* in either the hepatic or common ducts; (3) *stricture of the common duct, complete or incomplete, due to either ulcerative or inflammatory disease;* (4) *pressure of growths within the intestine or ducts* causing sufficient obstruction to prevent the onward flow of bile; (5) *extra-hepatic pressure* from tumors of the liver itself or growths in the surrounding organs including cancer of the stomach or pancreas, or both at the same time, kidney growths, malignant disease of the omentum, glandular enlargements in the portal fissure of the liver, enlargement, either benign or malignant of the gall-bladder, mobile kidney, abdominal aneurism, either aortic or celiac, perihepatitis or any pressure from whatever cause which is sufficient to obstruct the free flow of bile.

Bile is normally secreted at very low pressure; relatively insignificant increase of this pressure makes absorption of bile pigment into the blood easy and jaundice results.

Catarrhal Jaundice (Gastroduodenocholangitis).—In considering the diseases of the stomach we mention jaundice as one of the symptoms of catarrhal gastro-duodenitis. In most cases in which jaundice develops there is more or less *cholangitis*, the larger ducts are involved by extension from the duodenum. The majority of these cases are found in young subjects in whom the jaundice follows error of diet, and a short period of gastro-intestinal symptoms. The features are characteristic of obstruction and include besides the yellow-tinged skin, discoloration of the internal organs and secretions, the conjunctivae and mucous membranes, with a slow pulse and respiration, subnormal temperature, clay colored stools and constipation; bile laden urine, pruritus; in obstinate and severe cases petechiae and cerebral symptoms. *Simple uncomplicated catarrhal jaundice* or *gastroduodenocholangitis is usually a self-limited process which runs its course in from a few days to several months.* In but few cases does jaundice persist beyond three or four weeks, but it may happen that the obstruction remains and continues the symptom beyond the average time. Such cases are associated with more or less stomach and intestinal symptoms and loss of weight with weakness. *Convalescence* is slow, but complete restoration to health is the rule.

Influencing Factors

Urine.—The urine offers evidences of value for prognosis. With obstructive jaundice scanty and high colored urine is evidence of an active process; with increase of urine and the usual change to a lighter color from day to day, the prognosis for prompt recovery is good. The persistence of jaundice (usually fading) after the urine has cleared, is not unfavorable. *Leucin* and *tyrosin* are always unfavorable, they indicate grave and destructive disease.

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Indicanuria is not unfavorable. *Casts* and *albuminuria* are frequent, and with the positive diagnosis of catarrhal obstruction—uncomplicated—do not as a rule influence prognosis unfavorably. *Transitory glucosuria* in catarrhal jaundice is frequent and of no great significance.

Feces

The feces when "clay colored" prove the absence of bile from the intestine. The return of normal color is coincident with the removal of the obstruction.

When jaundice is due to *congestion of the liver secondary to disease of the mitral valve* or to *infections,* as *pneumonia or typhoid fever,* the prognosis depends almost entirely upon the gravity of the primary disease.

The infections and organic diseases in which jaundice may be a prominent symptom are separately considered. *The presence of jaundice with any infection proves extension to the liver or bile passages and is of great prognostic significance.*

Jaundice with puerperal eclampsia is almost always fatal. With malarial infection (See Section I) it is significant but not always grave; with relapsing fever it is ominous; following or associated with *acute abdominal lesions* as *appendicitis*—it is unfavorable in 55 per cent of cases (Reichel). In a relatively large number of cases swelling spreads from the small intestine (duodenum) to the head of the pancreas sufficient to obstruct the common bile duct; the jaundice disappears as the pressure is relieved.

In a few cases the infection causes *chronic catarrhal jaundice;* the bile passages, including the gall-bladder, are involved. Free drainage may be necessary to effect a complete cure.

Deep jaundice, with or without cerebral symptoms, *severe itching* and *petechiae* are symptoms of the more severe types of the disease and in diagnosis should lead to the suspicion and differentiation of malignancy or other organic change. It is not impossible, however, to find these symptoms in uncomplicated and severe catarrhal jaundice which recovers after a varying period and slow convalescence.

Jaundice with marked liver insufficiency and evidences of toxemia, including marked nervous manifestations (delirium, somnolence, and deep coma) and *hemorrhagic diathesis* offers an unfavorable forecast; *cholemia is the paramount factor in this syndrome. Nervous symptoms and jaundice usually indicate some grave underlying condition.* There are cases of *infectious jaundice with meningeal symptoms* during a few days, with final full recovery without disagreeable or persisting sequelae (Guillian and Richet). Rolleston has called attention to the similarity of these cases to epidemic cerebrospinal meningitis.

Slow pulse with lowered arterial tension, subnormal temperature,

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slight albuminuria, yellow vision and slightly enlarged liver, or palpable gall-bladder, are not unfavorable in the absence of complications. *Unchanging jaundice with loss of flesh and evidences of increasing weakness, whatever the initial symptoms, justify the conclusion that the obstruction is likely to be of malignant or organic nature and demands thorough differentiation before prognosis is given. With cancer of the liver, jaundice once present persists and is not modified by any treatment.* It only rarely happens that catarrhal jaundice complicates malignant diseases of the liver or pancreas; it is safe to cling to the rule that with *malignancy the jaundice is persistent and deepens as the primary disease advances.*

I elsewhere consider the infectious type of jaundice known as *Weil's disease* (See Section I).

The occurrence of *epidemic catarrhal jaundice* is possible. Large numbers may be infected within a limited area at the same time; the prognosis of such infection is almost uniformly good; recovery follows in from seven to ten days in average cases.

The jaundice associated with *impacted gall-stone,* either in the hepatic or common ducts, usually offers a good prognosis. In the majority of cases the obstruction is overcome either by nature's process or by surgical interference. There is under such conditions, always danger of ulceration, infection and suppuration; these complications are elsewhere considered (See Gall-stones).

Jaundice due to organic stricture of the common duct, complete or incomplete, following ulceration or inflammatory disease, *pressure of growths within the intestines or ducts,* can only be overcome by surgical interference unless of specific origin.

Tumors of the liver itself, or *growths in the surrounding organs* including *cancer of the stomach or pancreas, or both, and pressure from other sources* already mentioned as causes of jaundice, only offer a favorable prognosis when the growth is removable. The larger number of these conditions are not operable.

Chronic jaundice may lead to multiple *xanthoma* (xanthelasma or vitilligoidea). In these cases the cause is not removable. *Xanthoma may occur without jaundice.* Xanthoma is evidence of chronicity and non-malignancy as a rule. Chauffard considers xanthoma due to excess of cholesterin in the blood.

Chronic jaundice offers a grave prognosis. Surgical interference is not well borne. Hemorrhage is likely to occur and is not easily controlled. In chronic jaundice the *functional activity of the kidney is an important factor; when sustained, the prognosis is thereby improved.*

Deep jaundice, also chronic, known as *black jaundice,* due to the presence of biliverdin is usually of malignant origin. In occasional cases *leukoderma* complicates chronic jaundice due to carcinoma (Warthin

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and Rolleston). Deep jaundice persisting from any cause is always ominous.

(*b*) *Hemolytic Jaundice—Toxic Jaundice*

(*Hemo-hepatogenous Jaundice*)

It is now assumed that all forms of jaundice whether "obstructive" or "non-obstructive" as the older writers characterized them, are in truth hepatogenous. It has been abundantly demonstrated that the formation of bile pigment from the blood coloring matter of destroyed (fragmented) corpuscles outside the liver is usually limited to the liver cells, and according to most authorities does not take place in any other organ of the body; hence all forms of *hemolytic jaundice* are in reality *hemo-hepatogenous* (Moleschott, Stern, Minkowski, Naunyn and Stadelman).

Hemolytic jaundice according to Eppinger is obstructive, because with the destruction of the red blood corpuscles there is an excessive amount of hemoglobin which in the end provides for increase of bilirubin; there is plugging of the smallest bile ducts and change in the epithelial cells with increased viscosity of the bile. Thrombi in the bile passages and in the capillaries of the liver are common. The intrahepatic bile stasis and rupture of intralobular biliary capillaries, with entrance of bile through the lymphatics, are the changes which follow hemolysis which leads to jaundice.

Ogata has demonstrated the possibility of jaundice before the rupture of the intralobular capillaries, and he believes that it is possible to convert hemoglobin into bile coloring matter in the blood current or in the spleen; this view has not been generally accepted, though Whipple and Hooper have experimentally demonstrated the rapid transformation of hemoglobin into bilirubin in the blood current outside the liver. Eppinger claims to have demonstrated the production of lymphatic tissue at the peripheral end of the common duct in these cases of hemolytic jaundice, which prevents the free exit of bile.

It is exceedingly difficult to offer positive evidence which explains the method or seat of blood corpuscle destruction. It has been established by Chauffard (1907) that the red blood corpuscle undergoes hemolysis in an abnormal manner when exposed to hypotonic saline solution; "normally hemolysis of the red blood corpuscle begins in 0.42 per cent NaCl solution and is complete in 0.3 per cent"; in hemolytic jaundice "it begins at 0.6 per cent and is complete at 0.42" (Rolleston). This fragility of the blood corpuscles is characteristic of hemolytic jaundice when a disease *sui generis*, and is not present with hemolysis of pernicious anemia nor the intoxications including lead poisoning.

The influence of the spleen on hemolytic jaundice has received careful consideration in connection with splenectomy. It has been demon-

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strated that removal of the spleen in Banti's disease and in the familial types of jaundice has overcome all symptoms with restoration of normal blood conditions (Kahn, McPhedren, Fletcher and Harold Orr).

Hemo-hepatogenous jaundice may be a symptom of:

1. Infectious disease
2. Poisons and drugs
3. Cerebral disturbance
4. Sudden hemolysis, non-infectious or toxic
5. Splenomegaly.

Causes of Hemo-hepatogenous Jaundice.—1. *Infectious Disease.*—The prognosis of jaundice of hemolytic origin with the infections is always exceedingly grave, for it is idicative of malignancy. The infections which hemolytic jaundice may accompany are yellow fever, typhoid, typhus, malarial, relapsing fevers, septicemia, pyemia, scarlet fever, pneumonia, Weil's disease, and acute yellow atrophy of the liver.

2. *Poisons and Drugs.*—These include snake bites—exceedingly grave; phosphorous antimony and other mineral poisons, chloroform and ether, potassium chlorate, coal tar products, chloral, santonin, male fern, toadstools, copper sulphate, carbolic acid, pyrogallic acid and ptomain poisoning. The prognosis of these poisonings varies in the individual cases depending upon prompt detection of the poison and its treatment, the size of the dose, the resistance of the patient and many associated factors, each requiring separate consideration.

3. *Cerebral Disturbances.*—In the reduced and predisposed, sudden mental emotion or cerebral injury may be promptly associated with hemolysis and jaundice. The prognosis depends entirely upon the severity of the brain lesion when this exists, and the constitutional disturbance; with mental emotion as a cause, the prognosis is usually good when uncomplicated.

4. *Sudden Hemolysis (Non-infectious or Non-toxic).*—There are cases in which after *periodic hemoglobinuria* following exposure to cold, jaundice develops. When without nephritis, usually tubular, or the hemorrhagic diathesis, the outcome is favorable. The majority of these hemaglobinurias are due to existing, often latent nephritis, and it is not unusual to find hemolysis recurring after each exposure, until finally the symptoms of chronic nephritis are fully developed and death results from the usual causes which end the lives of nephritics.

Jaundice following transfusion of blood is of no great prognostic value; the outcome will always depend upon the nature of the disease demanding the added blood elements.

5. *Splenomegaly.*—Splenomegaly with hemolytic jaundice include familial and hereditary types, and according to Rolleston the *chronic infective jaundice of Hayem.* The general features of obstructive jaun-

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dice are missing; there is absence of bile from the *urine* (*acholuria*) and the *feces* are normal colored. Rolleston insists that the familial types of jaundice are an exception to the rule which insists on obstruction as the cause of all jaundice, for the evidence, he holds, is conclusive, which proves the production of bilirubin in the blood current. The fragility of the red blood corpuscles as shown by hypotonic salt solutions is characteristic.

(c) *Hereditary Splenomegalic Jaundice*

Chronic splenomegalic hemolytic jaundice may be either *hereditary, congenital or familial,* or in occasional cases it may prove to be acquired (Rolleston). Benjamin and Sulka have reported family jaundice which appeared after birth in one generation and congenital in subsequent generations. The disease may be hereditary and congenital or hereditary without being congenital. In occasional cases there is no enlargement of the spleen.

The *acquired hemolytic jaundice* may follow infection; it is *usually syphilitic.* This represents the type described by Hayem who unhesitatingly declares in favor of the specific origin of the disease in spite of repeated negative Wassermann reactions. The prognosis of the acquired or *Hayem infections type—usually specific*—is favorable. The prognosis of the congenital, hereditary and familial type, is not unfavorable for life; these subjects may live to old age without subjective complaints though they are without resistance to disease or traumatism and they never lose their jaundice.

(d) *Icterus neonatorum*

Jaundice in the newly born may be either (1) physiologic, (2) infectious, (3) of the grave familial type, (4) obstructive due to organic lesions in the ducts or liver.

1. Physiologic Icterus.—Physiologic icterus, or the usual *icterus neonatorum,* also known as *yellow gum,* is found in the majority of babes soon after birth; it is hemo-hepatogenous and offers an excellent prognosis, for in a few (2 to 3) days without annoying complications the skin clears and all evidences of icterus disappear. From 40 to 85 per cent of all infants become jaundiced during the first four days of life.

At the Sloane Maternity Hospital in New York City, 300 of 900 births showed jaundice; 88 were intense, and 212 mild (Holt). Stevens made a collective investigation of 2,086 children of which 1,212 were icteroid—58.1 per cent. Jorak in 248 newly born babies found icterus neonatorum in 80 per cent. The important point to decide in offering the prognosis of icterus of the new born babe is whether the process is

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physiologic or infectious, and in occasional cases two or more days may elapse before differentiation is possible.

2. Infectious Icterus neonatorum.—Infectious icterus neonatorum is rarely of the catarrhal variety or what Rolleston has characterized as "*mild infectious jaundice.*" Skormin found but three recorded cases. Thompson says that new born infants may be very ill with catarrhal jaundice and yet they recover as a rule.

The *severe infectious jaundice of the new born is usually of umbilical origin—suppurative umbilical phlebitis.* The complication is preventable, is often conveyed from the mother—when it is likely to be streptococcic and has a very high mortality.

Unfavorable features are high fever, rapid pulse, evidences of suppuration, gastro-intestinal symptoms, cyanosis, great unrest, and infection of several organs. There are at long intervals *epidemic forms of infectious jaundice* among the new born in which there are marked hemorrhagic symptoms. In these epidemics almost all die. Winckel reports 24 cases with 23 deaths. In most severe and malignant jaundice of the new born the infection is associated with the symptoms of septicemia and purpura, multiple embolic infarct, and acute fatty degeneration of the liver and other organs (*Buhl's disease, also Winckel's disease*).

3. Grave Familial Type of Icterus neonatorum.—Grave familial type of icterus neonatorum attacks successive infants of the same mother—all of these die. I had four consecutive cases, children of one mother all of whom died within four days of birth. The first child born to this mother was perfectly well, never jaundiced and grew to manhood. There was no history of similar disease in the ancestors of these parents nor among the brothers or sisters.

Arkwright reports a series of 14 cases in one family—the mother of these infants had jaundice when four years of age.

Glaister reports that all of Morgagni's children, 15 consecutive births, had icterus neonatorum.

4. Obstructive Icterus neonatorum Due to Organic Lesions in the Ducts or Liver.—Congenital obliteration of the bile ducts has been fully described by John Thomson who reported 50 cases; and Howard and Wolbach gathered the reports of 76 post mortems. Rolleston offers two explanations: (I) "that there is in the first place a developmental aplasia or a narrowing of the duct which gives rise by obstruction to cirrhosis; (II) that there is first a mixed cirrhosis of the liver which gives rise to a descending obliterative cholangitis."

In practically all cases examined microscopically by Thomson and Rolleston, cirrhosis was present. Rolleston says: "To sum up it is reasonable to believe that the disease is primarily started by poisons derived from the mother and conveyed to the liver of the fetus, and that a mixed cirrhosis and cholangitis are thus set up. The cholangitis accounts for

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the jaundice and by descending to the larger extrahepatic bile-ducts, induces an obliterative cholangitis analogous to obliterating appendicitis." In the unfavorable cases the occlusion of the ducts is absent, as death takes place early in life from congenital cirrhosis—if such cases live occlusion finally results.

Death may result during the first week of life from either umbilical or other hemorrhage. Of Thomson's 49 cases, 30 lived beyond the first month and of these 16 lived more than four months; 2 lived "into the eighth month." Laveson collected 62 cases; of these but three lived 8 months, and of these 1 lived 11 months.

Infection and *hemorrhage* claim most infants. Only the gloomiest prognosis is justified. There are, as Treves and Ashley have demonstrated, cases with only limited changes which remain latent for years, finally there is gradual cicatricial inflammatory occlusion.

Hereditary syphilis of the liver and bile passages is a cause of icterus neonatorum. Many of these children die; a large proportion recover if radical treatment is promptly instituted. It rarely happens that *gall-stones* cause jaundice in the new born (See Gall-stones).

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2. Acute Yellow Atrophy of the Liver

Malignant Jaundice

General Statements.—Acute yellow atrophy of the liver is an infectious disease of adult life, occurring oftener in women than in men; the relative frequency with which it attacks pregnant women is surprising. It is characterized by atrophy and degeneration of the liver cells, probably autolytic (Flexner) and is usually fatal.

Legg found that Baillon (Ballonius) reported a case in 1616; Bright in 1836 described and illustrated the disease, and in 1842 Rokitansky gave it its present name.

Acute atrophy of the liver is a very rare disease; in an active hospital experience I have during the past thirty years seen but 2 cases, and in private practice during an equal time I do not recall more than 3 cases. Among my last 6,300 internal diseases tabulated in private practice I failed to find a single case of malignant jaundice. In 21,682 medical cases at the Johns Hopkins Hospital, Thayer reports but 3 cases. Rolleston has seen 11 cases post mortem in twenty-seven years.

Symptoms.—With the rapid destruction—degeneration of liver cells—the *evidences of overpowering toxemia are prominent early*, and the symptoms referable to the nervous system—delirium and coma, in young subjects convulsions—with jaundice, are suggestive with the physical signs of decreasing liver dullness of the gravity and nature of the process. There are cases in children, though these are exceedingly rare. The usual age is between twenty and forty years—my last case was sixteen years of age.

The symptoms which brand the disease and which make prognosis possible before the end of the first twenty-four hours in the majority of cases, are early obstinate vomiting, greenish skin and conjunctiva, hemorrhagic symptoms—hematemesis, melena, petechiae—followed by the

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prompt invasion of the sensorium and rapid wasting, weak heart, and urinary changes, including *leucin, tyrosin* and *albuminuria* with *scanty urine,* tinged bile, and in some, almost complete suppression. *Some enlargement of the spleen* is the rule; the *heart and kidneys show the degenerative changes of malignant infection.*

Origin.—*The atrophic and degenerative congenital liver changes are probably without exception of luetic origin.* The acute syphilitic liver changes are considered elsewhere (See Syphilis of the Liver, Section I). Weber in 1909 found 53 cases of acute yellow atrophy of syphilitic origin in medical literature, and Fischer reports 50 collected cases of which four-fifths were females. These cases are not true cases of acute yellow atrophy, they may run a long course and occasionally recover and should be classified as *icterus gravis.* Unquestionably preceding infection and worry or mental emotion, as well as alcoholic excess, invite acute liver atrophy.

Ballin and Torek both report fatal cases of the disease after surgical operation and anesthesia. Torek reports its occurrence after the use of anesthol, a combination of chloroform, ethyl chlorid and ether.

Fatal acute atrophy of the liver may develop after chloroform anesthesia; evidences of degeneration are not immediate. These cases are exceedingly puzzling. One such with complete yellow atrophy Fischer of Frankfurt demonstrated in 1914 which followed an operation for appendicitis in a boy. Brackel's experiences are also worthy of study in this connection (See References).

Atrophy, acute and fatal, may develop in occasional cases of cirrhosis of the liver, catarrhal jaundice, hyperemia and gall-stones. The incidence is exceedingly rare.

Acute phosphorous poisoning is not identical with acute yellow atrophy though the subjective features are strikingly similar. Pathologically the differences are positive. With phosphorous poisoning the fat in the liver reaches 30 per cent and more, the size of the liver is increased; with acute atrophy there is but five per cent of fat in the organ and atrophy is its fate (Rolleston). The blood shows abnormal concentration with a high red count and moderate leukocytosis. Grawitz reports 5,150,000 red blood corpuscles and 16,000 leukocytes, while at the Massachusetts General Hospital the count averaged 5,520,000 reds and 12,000 whites with 60 per cent hemoglobin. Blood cultures have thus far failed to enlighten the clinician. Libman and White report negative culture, and Vincent found the colon bacillus in his case.

There is marked *acidosis and fixation of ammonia* by the organic acids, the liver being unable to transform the ammonia into urea. Urea is reduced and the percentage of ammonia is increased in the urine.

The *total nitrogen loss is increased because of the autolysis of the liver cells,* and the ammonia accounts for at least twenty per cent of the

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total nitrogen, whereas normally it accounts for only five per cent. I have not seen the cases of prolonged and subacute liver atrophy described by some writers (MacDonald and Milne). These are likely to be due to cirrhosis with enormous destruction of liver cells or to subacute hepatitis, and ought not to be considered acute yellow atrophy.

Forecast.—Cases with positive symptoms lifting the diagnosis above doubt offer an unfavorable forecast. My experience does not include a single recovery. I agree with Rolleston who says: "Some doubt would always arise as to the nature of cases that recover completely." The regenerative power of the liver which is certainly paramount when there is a remnant of liver cells to proliferate, may in rare instances make recovery possible. In these cases there is a compensatory hyperplasia which may save life, but recurrence and advancing degeneration may ultimately lead to death.

The prognosis, bad at all ages, is slightly better in children than in adults. Pregnant women offer only the gloomiest prognosis. Once the kidney function is seriously disturbed—and this is a part of the toxic and degenerative process—in most cases the outlook becomes correspondingly bad. Legg's list includes 28 cases, 4 reported recoveries; and Wirsing collected 15 non-syphilitic cases of recovery.

Duration.—The duration of the average case of yellow atrophy is less than four days. Some live into the second week; only a few become subacute. The chronic course casts doubt on the diagnosis as already suggested.

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3. Circulatory Disturbances of the Liver

(a) *Congestion of the Liver*

(*Hyperemia*)

In all forms of congestion of the liver the prognosis must be based on its cause.

i. Active Hyperemia

Active hyperemia is purely physiological during the process of digestion, and is pathological in such conditions as cause increased supply of blood to the liver, either as the result of *vascular paralysis* or *true plethora,* i. e., *polycythemia.* The prognosis of this condition as it occurs with the various infections (diphtheria, malaria, typhoid and typhus fever, etc.) has been separately considered.

There are in all probability a limited number of active hyperemias arising from faulty diet and improper living in which judicious and temperate habits with proper exercise lead to prompt recovery without remnant of organic change.

ii. Passive Hyperemia

Passive hyperemia is always a secondary process; it is rarely recognized during its incipiency, but in the advanced stage presents characteristic changes which prove the obstruction in the portal system. The leading primary lesions are *cardiac* and *pulmonary.* There are other factors which may lead to chronic congestion of the liver, including *aneurismal pressure, growths,* which cause pressure on the inferior vena cava, *occlusion of the hepatic veins, obstruction of the portal vein, or thrombosis.* Rolleston includes *malignant growths or hyatid cysts, pleural and pericardial effusion, pericardial and mediastinal adhesions.* The prognosis of hyperemia in these conditions naturally depends on the ability to remove the cause.

The *cardiac lesions which cause secondary hyperemia of the liver are usually valvular, in which compensation is faulty.*

Mitral obstruction and regurgitation and *diseased myocardium* are the leading lesions which cause backward pressure, with consecutive *tricuspid insufficiency* and chronic liver engorgement. *Tricuspid stenosis* may cause marked secondary hyperemia; it almost always follows mitral obstruction. With *mitral stenosis* there is, after a varying period, persistent venous engorgement, with characteristic enlargement of the liver which persists and leads to consecutive organic changes. *Mitral stenosis* is probably the most powerful cause of the "cardiac liver."

The *acute infections* may also cause liver congestion depending upon

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myocardial degeneration and sudden dilatation. The *pulmonary lesions* which cause chronic hyperemia of the liver are *chronic emphysema* and *asthma, chronic bronchitis, interstitial pneumonia, the pneumonokonioses, and occasionally pulmonary tuberculosis.* The damage to the liver depends entirely upon the degree and duration of the venous stasis. Early, the liver is enlarged and the capsule tense; as the condition remains and becomes chronic there is more or less productive change, final atrophy and shrinking, with the usual symptoms of portal obstruction. With heart lesions, the hyperemia may always be considered to be permanent, and if the patient lives, the secondary changes in liver tissue are sure to follow. The prognosis of cardiac and pulmonary conditions is unquestionably unfavorably influenced by the secondary changes in the liver, but it depends more upon the ability of the heart to compensate for the primary anomaly than upon any other factor.

Secondary hyperemia with persistent gastro-intestinal symptoms, which are proof of engorgement of the entire portal system, offers an unfavorable prognosis for life; with cardiac dyspnea and associated dropsies there is usually congested kidney and evidences of overpowering toxemia and weakness. *Ascites* is an unfavorable symptom, though in some cases, under treatment, the tone of the heart may be sufficiently improved to prolong the lives of these patients.

With mitral obstruction and insufficiency it is not at all uncommon to follow patients during many years who live in comparative comfort with *chronic painless enlargement of the liver.*

Persisting jaundice with passive congestion of the liver is always unfavorable, and is found in the most severe cases. The deeper the coloring the more threatening is the complication. *Jaundice with cyanosis is always unfavorable.*

The *urine* gives valuable data for prognosis in all primary heart, lung, and other conditions associated with congested liver.

Concentrated, scanty, albuminous, bile-laden urine with casts or without, urobilinuria, acidosis, leucin and *tyrosin,* is always ominous and justifies the conclusion that death is imminent in most cases. With the gradual increase of hyperemia and consecutive organic changes in the liver substance, a degree of tolerance may be established with regenerative and compensatory changes sufficient to prolong life during indefinite periods until the *right heart* finally yields.

When the organic changes are sufficiently advanced in the liver as to cause marked cirrhosis and atrophy, conditions exist which, according to Hunter, "may be said to have an independent existence," and such advanced changes make the prognosis exceedingly grave. It is often surprising how many years patients with chronic heart and lung lesions (emphysema, asthma, chronic bronchitis) live without change in the size of the enlarged and engorged liver. With *enlarged and pulsating liver*

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associated with tricuspid insufficiency, improvement of secondary symptoms is not to be expected. The pulsation remains to the end (Mackenzie).

Infection (pneumonia, pleurisy, malignant endocarditis) is a frequent cause of death. In a number of my cases the infection has followed along the bile passages from the intestine; *icterus gravis* has resulted, and death has promptly followed.

The association of *purpuric* or *hemorrhagic symptoms* with or without jaundice, delirium, coma, convulsions, the typhoid state with increasing myocardial weakness, are among the most unfavorable features.

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(*b*) *Diseases of the Portal Vein*

Pylephlebitis

(*Pylethrombosis, Adhesive Pylephlebitis;*

when suppurative:

Suppurative Pylephlebitis, Portal Pyemia, Multiple Abscesses of the Liver)

Pylephlebitis is an inflammation of the wall of the portal vein or one or more of its branches with thrombosis or final suppuration. The majority of all cases are associated with primary systemic infection in which the blood shows characteristic changes.

Thrombosis of the portal vein may follow long continued inflammation of the vein, change in its coats, calcification, phlebitis, or syphilitic deposit. Thrombosis may be due to extension of inflammation, i. e., infection from neighboring or distant organs. Thus with ulcer of the stomach or intestine, cancer of the stomach or pancreas, cholecystitis—with or without gall-stone—cholangitis, liver abscess, pancreatic inflammation, appendicitis, pelvic abscess, puerperal or pneumococcus infection, diphtheria, distant or near thrombosis, there may be extension to the portal vein. Following surgical operation for infectious processes, portal thrombosis is a relatively frequent complication. If the causes of all portal thromboses were cautiously tabulated, the seat of the primary disease in the individual case would be found in one of many organs, and with innumerable infections. There is scarcely an organ from which

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portal infection may not spread. Portal thrombosis is frequent with *splenic infarct* and other *lesions of the spleen,* including abscess, trauma, infection and perisplenitis. With many grave forms, the spleen is markedly enlarged.

The *thrombosis of marasmus* is of infectious origin, and always secondary. Herringham says: "To sum up, it may therefore be stated that the great majority of the cases depend upon local conditions; that, whether of local or general origin, infection is the most probable cause in all but those in which the vein is invaded by new growth, or by multiple adenoma, and is not excluded even in these; and that in a few cases no explanation can be given."

The underlying infection is usually so malignant or serious as to threaten life; the added thrombosis increases the dangers, making recovery exceedingly rare. *With thrombosis and liver cirrhosis* the course is often subacute, the duration varying from several weeks to as many months. The same course is found with malignant disease of the liver. Cases in which there are peritoneal adhesions may persist during a number of months. A number of recoveries have been reported. In some of these reported by Lyons, Osler and Rogers, it is difficult to controvert the diagnosis, but a strong element of doubt is justified and I am fully in accord with Herringham when he insists that "where diagnosis is so certain, no case of recovery can be admitted which is not proved by subsequent dissection." The prognosis, however, is better than in pylephlebitis. Compensation of the circulation is possible in cases in which portal thrombosis is limited and progresses gradually.

Suppurative Pylephlebitis—Portal Pyemia—Multiple Abscess of the Liver

This condition, always infectious, is fully considered in this section with *Abscess of the Liver,* to which the reader is referred.

(c) *Diseases of the Hepatic Vein*

Complete occlusion of the hepatic vein is exceedingly rare; its only interest is pathologic, for it cannot be diagnosticated intra vitam. The symptoms of hepatic occlusion, thrombosis, or phlebitis, are rather indefinite but usually include pain, abdominal and epigastric, *gastro-intestinal symptoms,* vomiting; in the subacute cases, *ascites* with *enlargement of the liver,* which continues more or less tender; *jaundice* is not usual. All are supposed to die.

Thrombosis of the hepatic vein may be due to *new growths of the liver, cirrhosis, stricture,* or it may be a *part of a widespread thrombosis, including portal thrombosis. Growths by pressure* (*carcinoma, hydatids, gummata*) causing stasis lead to thrombosis. Rolleston includes *oblitera-*

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tive endophlebitis of the hepatic veins as a cause. *Embolism of the hepatic vein* is rare. Welch reported fragments of new growth in the hepatic vein in cases of primary carcinoma of the thyroid and abdominal organs.

(*d*) *Diseases of the Hepatic Artery*

The anomalies of the hepatic artery include:

Aneurism
Embolism
Thrombosis
Arteriosclerosis

and according to Rolleston: *Enlargement of the vessel.*

Aneurism.—Rolland reported (1907) 41 cases in medical literature of *aneurism.* The average age of Rolland's cases was 37 years, and the extremes were 83 and 14 years. The proportion of males to females was 3 to 1, and the average age in women was 10 years higher than in men—45 to 35 years.

Ulceration in the gall-bladder or bile ducts may erode the wall of the artery and cause aneurism; the rupture is usual into the biliary tract in such cases. *Gall-stones* are potent factors in causing these ulcerations. Naunyn and Schmidt have reported cases in which impacted gall-stones have finally opened into aneurism of the hepatic artery. Jaundice is usually a late symptom, and is due to pressure on the ducts. *Ascites* is not a symptom of hepatic aneurism.

Aneurismal dilatation of the artery is always fatal; death is usually due to perforation. Perforation may take place into the peritoneum, the bile passages, the gall-bladder, the portal vein, or into the stomach, or (rarely) into the intestine or pancreas. Infection of the bile passages and pancreas is an occasional complication. Ross and Osler reported a case of infected aneurismal sac, multiple emboli, and many secondary liver abscesses. Fully formed hepatic aneurism is incurable; not all die from it directly, but most do. Rupture and perforation into the surrounding organs are the leading causes of death. Hans Kehr has successfully removed an aneurism after ligating the hepatic artery.

Embolism.—*Embolic infarcts* may cause multiple abscesses. They are always fatal, are secondary to malignant endocarditis, carcinoma, sarcoma—the melanotic type particularly—and are occasionally present with tuberculosis.

Thrombosis.—Thrombosis of the hepatic artery is considered a "pathological curiosity" (Rolleston). I have never met a case. Lancereaux found a clot in an arteriosclerotic hepatic artery in a patient, aged 65, who had general atheroma and died of gangrene of the feet.

Arteriosclerosis.—Arteriosclerosis of the hepatic artery is a part

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of a widely disseminated process. Secondary atrophy of the liver results in some cases—fibrosis of the liver is not usual with hepatic arteriosclerosis.

Endarteritis obliterans may accompany cirrhosis of the liver; Rolleston holds that endarteritis deformans is more frequent.

Enlargement of the Hepatic Artery (Rolleston).—With carcinoma and other new growths the hepatic artery is at times enlarged; the same is occasionally true of advanced cirrhosis and chronic portal thrombosis.

In all vascular lesions of the liver, both the underlying causes and the vessel changes are so grave and far-reaching as to make the forecast bad. The length of life in the individual case depends upon the nature of the primary lesion and the local changes caused by the altered vessels and disturbed circulation.

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4. Cirrhosis of the Liver

(a) Multilobular Cirrhosis
(*Chronic Interstitial Hepatitis, Laennec's Cirrhosis*)
(b) Unilobular Cirrhosis
(*Hanot's Cirrhosis*)
(c) Pericellular or Syphilitic Cirrhosis
(d) Capsular Cirrhosis
(*Perihepatitis*)

All forms of liver cirrhosis are characterized by connective tissue proliferation and changes in the liver substance. In all there is, in spite of destructive changes, marked tendency to regeneration of the liver cells. Another favorable factor is the fact that the connective tissue, contrary to the rule, holds capillary vessels which permit of the passage

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of blood to the intralobular veins by way of the hepatic artery, which (in alcoholic cirrhosis particularly) continues liver function, including bile formation.

(*a*) *Multilobular Cirrhosis*

(*Laennec's Atrophic Cirrhosis, Portal Cirrhosis, Chronic Interstitial Hepatitis, Contracted Liver, Hobnailed Liver, Drunkard's Liver, Alcoholic Cirrhosis*)

Factors Which Influence Prognosis.—*Alcohol* is unquestionably the most frequent poison which causes cirrhosis of the liver taken in the form of whiskey, gin, and brandy. Beer may cause mixed forms of cirrhosis, but it is less likely to produce the multilobular type of cirrhosis than are the stronger spirits. It is rare to find Laennec's cirrhosis without the history of alcohol abuse; it is possible however—a fact of diagnostic as well as prognostic value.

The study of my material justifies the conclusion that the majority of atrophic cirrhoses were found with an alcoholic history. Whether the changes in the liver are primary or secondary, we cannot ignore the positive history of the habit and I cannot agree that there is danger of exaggerating the "importance of alcoholism" as a pathogenic factor. There are other factors besides alcohol which cause cirrhosis, and there are many ingested poisons, besides alcohol, as well as congenital and acquired factors which lower liver resistance and predispose the organ to degenerative and productive changes.

The spleen is under suspicion as a poison-producing organ of transcendent importance in causing productive changes in the liver. The telling results which follow splenectomy in Banti's disease in which there is co-existing cirrhosis of the liver, and the early enlargement of the spleen in some forms of hypertrophic biliary cirrhosis justify the strong suspicion and the hope that ultimately we may find that through the spleen the liver changes are invited or provoked, and that early splenectomy in cirrhosis may abort these. This entire question is still *sub judice*—no authoritative statement is justified. There are some facts connected with the spleen which are of importance and are positive. The spleen is enlarged in 80 per cent of all cases of portal cirrhosis of the liver (Klopstock). The spleen is small in the more rapidly progressive cases, with profuse hematemesis, also with those in which ascites develops early. To some of these facts I again refer in considering individual symptoms.

Faulty Diet.—There are unquestioned cirrhoses in which *faulty diet* and consequent *dyspeptic conditions*, long continued, are causative factors. Ingested poisons by irritation, as well as those due to fermentation in the intestinal tract, may lead to "dyspeptic cirrhosis." The early

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detection of such cases is by no means easy; the changes are insidious and are advanced before marked subjective or objective manifestations cause the patient to seek medical advice. Most of these cases run an exceedingly chronic course and are favorably influenced by rational treatment and proper living.

Etiology.—The question of *etiology of cirrhosis as it influences prognosis* is still uncertain, but it is positive that there are many poisons which may cause liver changes parallel with cirrhosis. The lesions may be limited or widespread. *There is a growing belief that cirrhosis of the liver in man is always of toxic origin.* Rolleston's conclusions in this connection are as follows: "Poisons may be absorbed either from the alimentary canal and reach the liver in a comparatively concentrated form, or they may travel to the liver by the hepatic artery and are then comparatively diluted. Ordinary cirrhosis in man is generally due to poisons traveling by the portal vein. Alcoholism is rather an antecedent condition than a true cause, and acts indirectly or in an accessory manner. The possibility that cirrhosis is definitely due to microörganisms must be faced; from analogy it is most probable, but at present it has not been certainly established. It is also highly probable that poisons, or perhaps microörganisms, reaching the liver by the hepatic artery, may give rise to cirrhotic changes." "As a result of destruction of the hepatic cells and absorption of their proteins into the circulation, hepatic antibodies, or cytolysins, are produced. These destroy the liver cells and thus a vicious circle is produced" (Fiesinger).

The disease may be found during childhood, this is rare; it is most frequent during and after middle life, in the male oftener than the female.

Mortality.—Hawkins' statistics show that "the annual death rate from cirrhosis of the liver in England and Wales rose considerably from 1871-1900, reaching 134.6 in the last year, but in the quinquenium, 1901-5, a fall of 121.2 occurred. In 1905 there were 4,008 deaths registered in England and Wales as due to this disease."

The mortality from cirrhosis of the liver in the rural districts of New York State, as shown by Hoffman's statistics, is lower than in the cities of the State. "The rates have not been subject to a wide range, for the minimum rate per 100,000 of population in the cities of New York State was only 19.3 in 1909, while the maximum rate was 22.2 in 1907. The minimum rate for the rural territory was 10.1 in 1900 and the maximum rate was 15.1 in 1907. In 1909 the rural mortality from cirrhosis of the liver was 69.9 per cent of the urban."

Of 91 male white cases of cirrhosis of the liver admitted to the Johns Hopkins Hospital at Baltimore, 16 died in the hospital—17.6 per cent. During the same period (1902-1911) 16 white females were admitted with one death in the hospital—6.3 per cent. During the same period 15 colored males with cirrhosis were admitted with 2 deaths while in the

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hospital—13.3 per cent, and 4 females with no deaths. The total number of white medical cases was 7,299 males, from 1892 to 1901, and 3,209 females, from 1902-1911, 8,213 males, and 4,186 females. Colored medical cases included 1,678 males from 1892-1901 and 442 females; from 1902-1911 there were 2,109 colored males and 650 females (Hoffman).

The average age of individuals who die with the lesions of cirrhosis but without symptoms during life is according to Hilton Fagge "five years higher than of persons dying of the disease." This fact is a strong argument in favor of the success of the "compensatory processes." Rolleston on the other hand says: "In my own figures there is very little difference between these two classes."

Rolleston's statistics gathered from 78 cases dying from cirrhosis show an average of 48.3 years; whereas in 87 patients who died from independent causes but whose livers were cirrhotic, the average age was 49.1 years.

In alcoholic women especially, death from cirrhosis is much earlier than in those cases in which there is no history of alcoholic excess. Naturally the prognosis of all portal cirrhosis depends upon the extent of the liver changes, including the destruction of the liver cells, the extent of connective tissue production, the changes in the capsule, the obliterative changes in the portal vein, and its branches, the secondary changes in the ducts, the amount of amyloid and fatty degeneration of the organ, the accompanying lesions in other organs—kidney, heart and blood vessels particularly—the habits of the patient and his resistance, besides the regenerative power and tolerance of the liver itself.

Additional Prognostic Factors.—*Latency.*—It is often surprising to find how long after initial symptoms and positive physical signs the disease may remain latent. The duration of these periods of latency depends upon compensation which results from the collateral circulation established between the branches of the portal veins and the systemic veins and the regeneration of the liver cells. I have followed cases which finally died of intercurrent disease or accident during many years, in which the cirrhosis was advanced as shown at post mortem, the patients having lived with but few or no symptoms of the liver lesions. Hanot and Gilbert believe that the compensatory changes during latency cause enlargement of the liver in the majority of cases. All agree that *cirrhosis is oftener latent in men than in women.* Rolleston does not believe that this is due to the greater frequency of the diseases in men than in women, "for the ratio of women to men is lower among the cases dying independently of cirrhosis than among the cases fatal from the direct effects of cirrhosis."

The *latency of the disease is an important prognostic factor.* If the diagnosis is made early, before the various processes are advanced and

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the habits of the patient are controlled, without complication or toxemia, the chances for long periods of latency are exceedingly good; limited changes in the organ under such conditions may not materially interfere with the general health or length of life.

Patients with advanced latent cirrhosis are subject to complications—pneumococcus and tuberculous infections particularly—which often end their lives. Such subjects do not offer normal or average resistance to disease or trauma. Cirrhosis of the liver in the majority of cases, because of the tolerance of the organ and long periods of latency, often the carelessness of the patient and faulty diagnosis, due to the prominence of gastric symptoms, is not diagnosticated, until the disease is far advanced and pernicious habits are thoroughly fastened.

Lesions in Other Organs.—The lesions in other organs than the liver have an important bearing on prognosis. Cirrhosis of the liver is often associated with far-reaching changes in the digestive tract with *organic lesions of the esophagus, stomach, intestines* and *pancreas,* besides the spleen, already considered. *Advanced pancreatitis* is frequent; the fibrosis of the organ is often so advanced as to be out of proportion to the changes in the liver.

Esophageal lesions include changes in the mucosa, epithelial thickening, dilatation and varicose veins, and ulceration. The rupture of an esophageal varix or ulceration may cause profuse and threatening hemorrhage.

The *stomach lesions* include *chronic gastritis* (alcoholic) *varicosities of the gastric veins* at the cardia, continuous with the esophageal dilatation or separate. These may rupture or ulcerate and prove life-threatening.

Single or multiple gastric ulcers are occasional complications. The multiple ulcers are usually superficial, the single gastric ulcer is not frequent. *Intestinal lesions* which are associated with cirrhosis include chronic enteritis with productive changes causing marked thickening of the mucosa and atrophic changes in the glandular structures. There is with these atrophic changes in the chronic cases diminution in the length of the intestinal tract. The venous system of the intestine is likely to be engorged and the rectal veins dilated with *hemorrhoidal swellings. Rectal ulceration and bleeding* may prove depleting.

Kidney lesions complicated the majority of our cases. In over 50 per cent of all cases the kidney is enlarged. Milian and Bassnet in 89 fatal cases of cirrhosis found the kidneys normal in 19; in 53, or 59.5 per cent, they were healthy or more or less hypertrophied. Pitt's statistics show that when otherwise healthy, the kidneys were hypertrophied in 50 per cent of liver cirrhosis.

Arteriosclerotic interstitial nephritis is present in at least one-fourth of all cases and with the general invasion of the arterial tree, and toxemia is serious. Sears and Lord in this series of 78 fatal cases of cirrhosis

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report chronic nephritis (interstitial or tubular) in 23—or 29.4 per cent, fatty change in 15, and lardaceous change in 2. Rolleston compiled 440 cases of cirrhosis of the liver from the statistics of Pitt, Kellynack, Yeld, Cheadle and his own, in which he found 110 "with distinct fibrosis of the kidneys (25 per cent)."

Non-tuberculous Chronic Peritonitis.—Sears and Lord in their series of 78 cases found chronic peritonitis in 19 per cent. In most cases this peritonitis is mild and insignificant; indeed by causing agglutination of peritoneal layers or folds it may often prove salutary. Severe or advanced and threatening chronic peritonitis is comparatively rare with liver cirrhosis. The peritoneum, according to Rolleston, may with ascites be irritated by the "toxic bodies or bacteria in the ascitic fluid"; . . . "and it is conceivable that occasionally they are both related to alcoholism." *Ascites with chronic peritonitis* may require repeated tapping, and recovery may at times follow. The prognosis following tapping without chronic peritonitis is less favorable than with it and death is more prompt. The latter cases rarely live to be tapped more than two or three times.

Chronic peritonitis has complicated a few of my cases. In some of these ascites was an early symptom, in others late. From 8 to 10 per cent of all liver cirrhosis show *tuberculous peritonitis.* Nineteen per cent of Sears' and Lord's cases of cirrhosis had *chronic peritonitis.* Kellynack's material included 121 cases of cirrhosis, of which 12 had active peritoneal tuberculosis. Only one-third of these failed to show tuberculous disease elsewhere in the body.

Pulmonary Tuberculosis.—Cirrhosis of the liver predisposes to tuberculosis and the lungs are the usual seat of disease. Not all cases of pulmonary tuberculosis associated with cirrhosis are active. There may be but few or no symptoms; the process may be latent during long periods. In a small number of cases there is an *acute and rapidly fatal course with all of the lesions and symptoms of miliary tuberculosis.*

Tuberculous lesions are found in the lungs of over 22 per cent of patients dying of liver cirrhosis as proved by the statistics obtained from 584 cases (Lancereaux, Kellynack, and Yeld). The addition of acute pulmonary peritoneal or intestinal tuberculosis is promptly fatal with fever, emaciation, and deep toxemia. *Chronic tuberculosis with cirrhosis* may cover a long history and if the latter is limited and the former not far advanced, under favorable conditions life may be materially prolonged (See also separate symptoms, etc.).

Arteriosclerosis, etc.—Syphilis, alcoholism and *cirrhosis of the liver,* coincident during middle life, naturally include arteriosclerosis. Probably arteriosclerosis and liver cirrhosis bear but little relation to each other, and cirrhosis *per se* is not likely to produce arterial degeneration. Most cases of cirrhosis unless complicated with coincident nephritis and arteriosclerosis are without suggestive arterial hypertension. ***Mixed***

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cases of alcoholic and syphilitic cirrhosis may include specific arteritis (endarteritis).

Arteriosclerosis is unquestionably present in the bodies of most cirrhotics but it is by no means essential; in many it does not directly influence prognosis. When advanced, involving the heart and kidney or mesenteric vessels, or when there are evidences of cerebral or spinal arterial degeneration, the prognosis is correspondingly bad.

The Heart.—The heart in the average cirrhotic during the early stages may remain uninfluenced. With increasing toxemia or neglect and advance of the process, renal invasion or other complications, such as tuberculosis or portal obstruction with ascites, the myocardium suffers and the prognosis is correspondingly bad. The frequent association of syphilis clouds the prognosis because of specific aortitis, coronary endarteritis, and degenerative changes in the heart muscle in many. *Malignant endocarditis, always fatal,* may be grafted upon the previously diseased endocardium, for *valvular lesions due to chronic cardiopathies are not infrequent.*

Calcified adherent pericardium is rarely found without cirrhosis of the liver. If extensive it may interfere very materially with the comfort of the patient and cause secondary and severe complications (Diemar, Wells, Mitchell).

Cancerous Infiltration.—The prognosis of cirrhosis promptly becomes bad when there is *cancerous infiltration of the liver or other organs.* The cases reported as *primary cancer of the liver with cirrhosis* are (according to modern pathologists), cirrhosis primarily, with ultimate secondary proliferation—"hyperplasia of the liver cells." These conditions have been variously described as *"primary carcinoma with cirrhosis,"* "malignant adenoma," "cirrhosis maligna," and "cirrhosis carcinomatosa" (See Sabourin, Hanot and Gilbert). Rolleston says that since the malignant change follows the cirrhosis, as carcinoma of the breast follows chronic mastitis, "or on the analogy of carcinoma supervening on gastric ulcer," it would be better to speak of the condition as *"cirrhosis carcinomatosa."*

Individual Symptoms.—I have purposely considered the complications and secondary changes associated with Laennec's cirrhosis before dilating on the prognostic significance of individual symptoms because it is a striking fact that the disease may exist during long periods without causing the slightest, or but few, subjective complaints; patients often die of intercurrent disease in whom cirrhosis was never suspected, in whom advanced lesions are found post mortem, while the symptoms of secondary changes or complications are prominent.

Cirrhosis of the liver, per se, barring secondary changes and complications is a disease with but few well-defined symptoms. Patients usually continue comfortable and are without threatening symptoms so long as

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the compensatory circulation is upheld and the regenerative processes are maintained. In no other disease is the compensatory influence of collateral circulation with pathologic changes more important than in liver cirrhosis. With the compression of the branches of the portal vein and resulting portal stasis, symptoms appear. The gravity of the condition depends upon the extent of the obstruction and the associated toxemia and the lesions in distant organs.

Weight.—Progressive loss of weight, with or without evident complication, is always unfavorable. The subjects of advanced cirrhosis are not likely to regain lost weight. As a rule some complication of grave import is added when with loss of weight, the general condition and resistance suffer. In the advanced cases, loss of weight is always indicative of progression toward the end. Tuberculosis and malignant disease or chronic toxemia may be responsible for the loss of weight. Obese patients with latent cirrhosis may develop acute tuberculosis which promptly becomes disseminated, in the presence of an enlarged liver. In some of these, cirrhosis may not be suspected. *Loss of weight at any time in the course of cirrhosis is unfavorable and demands thorough investigation.*

Facies.—Just as with ovarian tumor there is often a characteristic facial change and a striking expression (ovarian facies), so I have noted in cirrhosis of the liver, often before the disease is far advanced, facies exceedingly suggestive but difficult to describe. The face is thin, the eyes somewhat sunken, the conjunctiva congested, superficial vessels prominent—particularly about the nose—the lips dry, often cracked, the teeth are abnormally dry and often with little sordes; the expression, as the disease advances, appears anxious.

Venous obstruction.—When there are positive symptoms of obstruction of the branches of the portal vein it may be concluded that the fibrous changes in the liver are advanced and the outcome will be largely dependent upon the factors of safety already mentioned in this chapter. The tolerance of the liver and its compensatory changes may often prolong the lives of these patients during indefinite periods. I have seen life prolonged in comparative comfort after positive physical signs and subjective symptoms of liver cirrhosis—over twenty years in one case—in which the post mortem verified the original diagnosis; the patient died of stomach cancer.

Gastro-intestinal Symptoms.—The *gastro-intestinal symptoms* may be due either to primary *gastritis* or *enteritis,* or to circulatory obstruction. *Persistence of passive gastro-intestinal hyperemia is usually associated with marked disturbance of hepatic function; stomach intolerance and frequent vomiting are weakening.* Such cases are rarely free from toxemia and other circulatory symptoms which, unless promptly relieved, are likely to prove fatal. In the majority of cases the secondary gastro-

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intestinal hyperemia is well borne during long periods and is as a rule only a part of a symptom complex which includes changes in other organs of serious import. *Persistent diarrhea* in advanced cases is suggestive of ulcerative or tuberculous disease. *In incipient cases diarrhea may be due to associated catarrhal enteritis and is amenable to treatment. Diarrhea alternating with constipation is always suggestive of tuberculous peritonitis.*

Spleen.—The *enlarged spleen* is found in the majority of cases. It cannot be definitely asserted that it is always the result of secondary congestion for it is not at all unusual to find the spleen enlarged during the early stages of the disease before there have been sufficient primary changes to cause obstruction. The spleen is most likely to be prominent with advancing cirrhosis; during periods of latency it often recedes. *When during latency the spleen increases in size other evidences of progression are not long postponed; these include ascites, gastro-intestinal symptoms, hematemesis, a toxic state often, which is associated with profound nervous symptoms, and albuminuria with few or abundant casts. Persistent enlargement of the spleen after hematemesis is unfavorable; recurrence of hemorrhage, toxemia or ascites may be expected.* With obstruction there is, as a rule, *obstinate constipation* and the associated subjective symptoms including languor, anorexia, and often toxemia. Unless the disease is *advanced*, diet and rational treatment are fairly effective. With toxemia, ascites, intolerant stomach and obstipation, there are usually cardiovascular symptoms (myocardial insufficiency), characteristic facies, and death in coma is not unusual. In this class of cases *paracentesis of the abdomen for the relief of ascites is often promptly followed by the deep invasion of the sensorium and death.*

Caput medusae.—With closure of the collateral circulation the compensation of portal obstruction is reduced. As portal obstruction advances every collateral avenue is employed to return the blood to the right heart. The dilatation of the superficial abdominal veins is indicative of marked portal obstruction and failure of the collateral circulation to compensate. Blocking of the communication between the epigastric and internal mammary veins, usual with marked portal stasis, causes dilatation of the superficial veins around the umbilicus (wreath-shaped), and is known to clinicians as the "*caput medusae.*"

With marked ascites, there is obstruction in the portal circuit, stasis in the vessels of the lower extremities with consecutive distension of the inferior epigastric and internal mammary veins with consecutive superficial stasis.

Hematemesis.—The prognostic significance of hematemesis depends upon the stage of cirrhosis in which the bleeding occurs. When hematemesis is an early symptom it is not at all unusual, under favorable conditions, for the patient to live many years. Such histories are com-

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paratively frequent even in the presence of marked cirrhosis followed by latency. Early bleeding may prove a wholesome warning, which when heeded may prolong life. *Hematemesis in late cases*, with other evidences of obstruction, is unfavorable.

In advanced cirrhosis the first hematemesis may be profuse and fatal. *Hematemesis due to esophageal varix* may be fatal at once or there may be repeated small bleeding which with the co-existing toxemia finally deplete the patient. The prognosis of bleeding due to varices is worse than ordinary uncomplicated hematemesis.

Hematemesis with ascites or other circulatory embarrassment is always unfavorable.

Hemoptysis.—Hemoptysis has never in my experience been profuse in uncomplicated liver cirrhosis. When a symptom of the purpuric condition with advanced cirrhosis, it is unfavorable.

With hemoptysis due to disease of the nasal mucosa it is insignificant, *per se*.

When due to associated tuberculosis, the forecast depends on associated conditions and the amount of blood lost, and is easily made. *The majority who raise blood with cirrhosis are tuberculous.*

Hematuria with cirrhosis is either dependent upon purpura and a deep toxic state or nephritis. In either event there are likely to be hemorrhages from other sources particularly with purpura. *Acute nephritis* occasionally complicates cirrhosis and adds an element of danger.

Epistaxis.—Nose-bleed is frequent with cirrhosis. It may be one evidence of the purpura dependent upon hepatic insufficiency or infection, and is often counted among the symptoms of the terminal toxemia. Uncontrolled epistaxis may prove depleting. In the purpuric and profoundly toxic it alternates with bleeding from other surfaces—the kidneys, intestines (melena), or bladder.

Melena.—Intestinal bleeding early may be transitory and without significance. With advanced cirrhosis melena is always of serious import. When it follows hematemesis its significance is measured by the quantity of blood lost and associated conditions. Gastric and duodenal ulcers with cirrhosis may cause intestinal without gastric hemorrhage. Extensive rectal ulceration with profuse bleeding may cause death.

Hemorrhoidal bleeding is not, as a rule, of grave significance.

Purpuric conditions are evidences of profound toxemia and malnutrition, and with cirrhosis are promptly followed by death. In some cases bleeding from the gums or nose with small patches of necrobiosis may continue with chronic toxemia during a number of weeks before the end.

Change in the Size of the Liver.—It is exceedingly difficult to offer a forecast based upon the change in the size of the liver. Possibly it is safe to conclude that in the majority of cases the smaller the organ (the more advanced the contraction) the more unfavorable is the forecast. With

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latency, the prognosis is usually more favorable when the liver shows some enlargement, but its enlargement during this period may be the precursor of serious complication or advancing disease. Rolleston says: "But this is not a hard and fast rule, since enlargement may be temporary and due to alcoholic excess, to absorption of poisonous products from the alimentary canal, or to complications such as cardiac failure and backward venous pressure." The outlook is, however, always better with a large than with a small liver and most of my cases which fell into long latent periods or improved after tapping for early ascites had large livers.

Ascites.—Ascites should always be regarded as one of the gravest results of portal obstruction and unless it is an early symptom with an enlarged liver, without toxemia in a well nurtured and resistant patient in whom early paracentesis is followed by improvement, without recurrence, it offers an unfavorable prognosis.

With previous symptoms making the diagnosis of liver cirrhosis positive, and the development of ascites, the prognosis is absolutely bad and but few cases survive more than one or two tappings. Hale White makes the unqualified statement that cases of uncomplicated cirrhosis—without chronic peritonitis—never survive more than one paracentesis abdominis. This has not been my average experience. *There are cases of advanced cirrhosis in which tapping is promptly followed by a toxic condition and death within three or four days. No advanced case should be tapped without having this possibility in mind.*

It may be positively stated that by tapping in individual cases, in which ascites is an early complication, in which the liver is large, periods of latency or apparent recovery may follow. Cures have been reported by competent clinicians under similar conditions.

Ascites with cirrhosis due to mitral disease or chronic peritonitis offers a much better prognosis than does the dropsy which is entirely due to portal obstruction of productive origin. *Hemorrhagic ascites* is always less favorable than ascites with a relatively clear fluid. It may be evidence of chronic hemorrhagic peritonitis, rarely tuberculosis, or added malignant disease within the abdomen.

General Dropsy.—General dropsy (*edema of the legs, general anasarca*) is a terminal complication of cirrhosis and offers only the most unfavorable outlook. These patients are usually profoundly anemic and toxic with myocardial insufficiency and often show kidney invasion.

Urinary secretion.—So long as the urinary secretion remains sufficient to allow of free elimination and there is no serious or deep invasion of the parenchyma of the kidney, the prognosis is favorable, for it is a fact that with serious obstruction, profound toxemia or threatening complications, the urine is promptly changed and excretion proves insufficient. With rapid destruction of liver cells, acute exacerbation or serious

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interference with hepatic function, the urine is a valuable prognostic index.

Acidosis with fully developed cirrhosis is often acute and grave; *chronic acidosis* is less threatening, but is a part of the toxic process which is always of serious import. *A large increase in ammonia* (nitrogen in the form of ammonia) is often due to the destruction of liver cells and is unfavorable. *Marked increase in ammonia and decided decrease in urea are ominous.*

The presence of *leucin* and *tyrosin* in the urine indicates advanced liver cell degeneration and is therefore serious.

In the majority of uncomplicated cases there is but little *jaundice;* hence the urine is not surcharged with bile, as with the hypertrophic disease. The urine in the graver cases, usually in the advanced stage with obstruction, is concentrated; the quantity is decreased; there is increase of urates and uric acid; *urobilinuria* is almost constant.

Evidences of passive congestion of the kidney (albuminuria, few casts, red blood corpuscles) marks the period of portal stasis and is coincident with other secondary changes unlikely to yield to treatment. *Marked urea reduction with albuminuria* and *myocardial weakness* justify only the gravest forecast. *Occasional glucosuria* with limited liver changes during the early stage is not serious; it usually proves to be transitory. With *diabetes bronzè* (See Diabetes) the prognosis is always bad. *Persistent glycosuria* with marked stasis during the advanced stage is always ominous.

The combination of diabetes mellitus and liver cirrhosis in the alcoholic is serious, though with rigorous and rational treatment, without grave complications and in the absence of toxemia of any kind such lives may often be prolonged and made comfortable during long periods. Alimentary levulosuria is of some value in determining the extent or degree of liver insufficiency. The *increased toxicity of the urine* is a factor of considerable value in determining hepatic inadequacy (Roger).

Albumosuria may prove to be evidence of hepatic insufficiency; associated conditions demand serious consideration before its importance as a symptom is interpreted.

Uremia with cirrhosis and advanced stasis make a dangerous complex. Such patients die within a few days in *coma,* though *chronic uremia* may be present during a number of weeks or even months before *coma* or other complications end life; some of these patients yield to infection.

Jaundice.—Slight icteroid tint is frequent. Deep jaundice is the exception in uncomplicated cirrhosis. Moderate jaundice is found in about one-third of all cases (Rolleston). Slight or even marked jaundice may depend upon transitory cause, and disappear. With *acute exacerbation of gastroduodenitis* jaundice becomes prominent, to fade as the mucosa returns to its chronic condition. When with cirrhosis jaundice

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persists and is deep, it is an unfavorable feature, more particularly when with acute exacerbations liver cells degenerate and *icterus gravis* results.

Jaundice due to gall-stone impaction in the common duct may complicate cirrhosis. The prognosis, unless relieved by nature is less favorable than without cirrhosis, as *cirrhotics do not tolerate radical surgical interference so well as do normal subjects.* With such complication there is always great danger of added infection.

The Blood.—The blood picture offers a fair index of the general result of the liver changes and included toxemia. The latent and early cases which are favorable show but slight or no blood changes.

Progressive cirrhosis runs parallel with increasing secondary anemia. There is decrease in the hemoglobin and a lowering red blood count. Emerson reports counts between 3,100,000 and 5,000,000 in 32 cases with an average of 4,500,000; the hemoglobin average was 68. The hemorrhagic diathesis increases anemia very suddenly at times. When the secondary anemia becomes grave, normoblasts are found. I have records of a number of cases in which with depleting factors and toxemia the count fell to 2,000,000—in one case lower. Cabot reports a case with 1,200,000 reds and 22 per cent hemoglobin. Limbeck saw a case with 1,500,000 reds, while Grawitz offers no such low counts but agrees that with the secondary anemia there is moderate leukocytosis and that the specific gravity of the blood never falls below 1,040.

Leukocytosis is characteristic of cirrhosis; marked leukocytosis invariably makes the prognosis bad (Rogers). Marked *reduction of the alkalinity of the blood indicates acidosis, and is unfavorable.* This condition is frequent in advanced cases.

Tuberculosis.—I have elsewhere referred to the frequent *association of pulmonary tuberculosis and liver cirrhosis* and its baneful influence. *Acute miliary tuberculosis with cirrhosis* is rapidly progressive; with high fever, rapid pulse and emaciation, death may follow in from four to twelve weeks. In several cases in men of middle life the average duration was less than six weeks.

Chronic tuberculosis and cirrhosis may cover a long period. *Latency of both processes under favorable conditions is not impossible.* This is particularly true of *chronic fibroid phthisis* as well as of those forms in which there was previous latent phthisis with fibrosis, in which liver degeneration is not far advanced and in which environment and habits are favorable.

Active tuberculosis with cirrhosis of the liver always justifies a guarded prognosis and as a rule it is unfavorable. From 10 to 15 per cent of all cirrhotics die of pulmonary tuberculosis; 22 per cent of all cirrhotics show lesions of pulmonary tuberculosis on post mortem examination.

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Bronchitis.—The *chronic pharyngitis and bronchitis of the alcoholic with cirrhosis* are not of importance in prognosis, though often annoying. These conditions are likely to yield to treatment and abstinence. *The uncontrolled cough or persistent bronchitis of the cirrhotic patient should always arouse the suspicion of coincident tuberculosis.*

Pneumonia.—Pneumococcus infection is frequent; alcoholic cirrhosis invites it. Either croupous or catarrhal infection of the lung offer an ominous outlook. Pneumonia is likely to complicate streptococcus infection such as erysipelas in the subjects of Laennec's cirrhosis, and with delirium, often *meningismus* or *meningitis;* these patients die. Occasionally an alcoholic recovers from pneumonia in the presence of an incipient cirrhosis (See Pneumococcemia).

Pleurisy.—Fibrinous pleurisy is not frequent; it offers a good prognosis. *Pleurisy with effusion* is often tuberculous in cirrhotic subjects. Pleurisy with effusion is more frequent on the right side, due to the spread of inflammation from the liver through the diaphragm (Villain). Such effusion is likely to be bloody. In advanced cases the addition of pleural effusion or hydrothorax due to cardiac failure are serious, and never to be lightly regarded.

Invasion of Nervous System.—Most symptoms and complications referable to the nervous system are of toxic origin. Profound invasion of the nervous system—the brain particularly—is always grave and in most cases presages early death. During acute exacerbations there may be some evidences of mental hebetude which often yields with the relief of the toxic state.

Acute or chronic alcoholic poisoning, with exacerbations including mental disturbances, delirium tremens, stupor or coma is always serious in the course of an active cirrhosis. The milder evidences of toxemia, frequently present during the early stage of cirrhosis, including headache, lassitude, mental laziness, vertigo, tremor, and a variety of subjective complaints, yield to treatment and abstinence from alcohol.

Mental symptoms due to uremia and renal insufficiency are always grave. Renal insufficiency with cirrhosis of the liver promptly increases all nervous symptoms due to the resulting toxemia. *Coma suddenly or gradually developed at any stage of cirrhosis is a symptom of the gravest significance, and never justifies any other than a grave prognosis.*

There are occasional cases, as already suggested, in which coma proves transitory; these are exceptional, particularly when the cirrhosis is in an advanced stage. Coma is largely dependent upon renal and hepatic insufficiency. The prognosis depends therefore on the extent of the liver degeneration and the ability of the kidney to relieve the surcharged blood of its toxins.

Delirium tremens with alcoholic meningitis and cirrhosis of the liver usually ends fatally. I have in my service met cases of delirium tremens

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with wet brain which slowly mended. In a few of these I have found *peripheral neuritis* a sequel, from which recovery was usually slow.

It occasionally happens that a fully developed, or even incipient, cirrhosis is complicated by fully developed *peripheral neuritis* in which the prognosis of the latter complication has been fairly good when without associated depressing factors.

Convulsions during any stage of cirrhosis are serious. They usually depend upon grave underlying conditions; toxemia or pressure may precede meningitis or coma from which recovery is the rare exception.

Delirium with cirrhosis and active delirium tremens often includes pneumonia—a bad but frequent combination in hospital practice. Any form of *meningitis complicating cirrhosis* is serious and with increasing stupor and final coma leads to death.

Gowers, Wilson and Nammack have described cases of *"progressive lenticular degeneration"* in which there is mixed cirrhosis of the liver and symmetrical degeneration of the lenticular nuclei. The course may be chronic; the prognosis is bad. Gowers characterized the disease, which is usually familial, as *"tetanoid chorea."* The disease is not hereditary. *There is bilateral tremor and spasticity when the disease is advanced, dysphagia and anarthria without true paralysis.* The disease is not syphilitic and probably not of alcoholic origin but is due to a toxin; it is probably not microbic and possibly a lipoid; it exerts a selective action on the lenticular nuclei, comparable to the selective bile-staining of the lenticular nuclei in "kernicterus" (Rolleston).

Cerebral thrombosis, embolism and *cerebral hemorrhage* are all without encouragement for the future of the cirrhotic patient. These complications may occur during the latent or active periods of the disease.

Gout with its symptoms may materially influence the comfort and general health, and with associated heart lesions or kidney changes often proves a formidable complication. In but few cases does gout, *per se,* cause the death of patients with liver cirrhosis. The *influence of traumatism and resulting infection* on the lives of these patients is paramount. As we have already said *the average cirrhotic offers but little resistance to surgical interference; the same is true of trauma of any kind.* Surface injuries and fractures are likely to be followed by streptococcus infection (erysipelas often) and pneumonia.

Terminal infections are easily acquired and demand the greatest vigilance. Besides *erysipelas* and *pneumonia, malignant endocarditis, pericarditis, pachymeningitis,* and *kidney infection* are among the causes of death.

Temperature.—Slight elevation of temperature during the early stage of the disease is usually transitory and not significant. Persistent elevation of temperature is always worthy of investigation; its cause will

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at once make its significance clear and prognosis possible. With unexplained fever, tuberculosis should be suspected.

Pulse.—The pulse is always a valuable prognostic index with cirrhosis. *Persistently rapid heart* is indicative of some complication or *degenerative change of the myocardium.*

Heart.—Heart failure in cirrhosis is rarely sudden; the heart continues tolerant with a rapid pulse during surprisingly long periods. Rapid pulse with coma is almost always the precursor of the end. Marked *hypotension* with associated evidences of venous stasis and feeble pulse not infrequently continues during several weeks before death. The prognostic significance of *hypertension* depends upon associated conditions. Alone it is of but little value.

Respiration.—Hurried respiration may persist during weeks with advanced cirrhosis and ascites, or there may be tuberculous infection, pleurisy, or heart weakness. *Abnormally slow respiration* may be due to toxemia or to some central lesion.

Skin Lesions.—The skin lesions do not materially influence prognosis. *Obstinate pruritus* with or without icterus may prove annoying, but does not as a rule do more than cause insomnia and aggravate the other nervous symptoms. *Pain* is not sufficiently severe to depress or influence the patient seriously.

Pigmented Cirrhotic Livers.—Cirrhotic livers occasionally show characteristic pigmentation in which particles of carbon, metals, or stone find their way through the blood stream to the organ (*cirrhosis anthracotica*); hemorrhage during the course of cirrhosis may leave sufficient blood coloring matter to cause moderate pigmentation; with hemochromatosis and diabetes bronzé and with chronic malarial poisoning with associated cirrhosis, pigmentation is found (See Malaria and Diabetes Bronzé).

The prognosis of *hemochromatosis with pigmented cirrhosis and diabetes bronzé* is uniformly bad. The former patients may live during long periods but they die as a rule of gastro-intestinal hemorrhage, while in the latter the *course* of the disease is much shorter and death is rarely postponed beyond eight to twelve months.

The *malarial cases* are chronic as a rule. It is questionable whether malaria *per se* causes cicatricial change in the liver. Barker claims that existing conditions with severe malarial infection (the degenerative and necrotic changes in the liver parenchyma) are favorable for the proliferation of connective tissue in the liver. Osler has failed to find malaria causative of cirrhosis and the post mortem table strengthens Osler's contentions. Probably in these cases alcohol is the factor and the prognosis of portal cirrhosis must hold for that of the pigmented cirrhotic liver with the history of malaria.

The Influence of Surgical Treatment.—It occasionally happens that after repeated paracentesis abdominis ascites does not return and patients

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remain fairly comfortable during comparatively long periods. The repeated tapping or possibly wounding the liver may have caused adhesions around the liver.

The history of the surgical treatment of cirrhosis of the liver is interesting. The operation most popular is known as the "Talma-Morrison operation." Drummond and Morrison (1896) attempted to establish and increase the collateral circulation between the portal and the general systemic veins. Talma had originally planned the operation in 1889, and Van der Muelin in 1889 did the operation. He was followed by Schelkley in 1891 and by Lens in 1892. The operation has for its object an examination of the peritoneum to determine whether the existing ascites is due to chronic peritonitis; if it is, the operation is useless. Then the peritoneal surface over the liver is scraped to provoke adhesive inflammation and the surfaces are brought together by stitching the round ligament to the abdominal wall or by running the stitches through the liver. In some cases the greater omentum is used to increase the vascular adhesions, and it is held between the diaphragm and the convex surface of the liver. Pathologists hold that the improvement in the condition of the patient is not due entirely to the increased collateral circulation, for it has been shown that this may cause deep toxemia experimentally; but that there must be some other explanation.

Thomson has contended that the improvement is due to the obliteration of the peritoneal cavity by adhesions, and Rolleston and Turner held that the benefit of a collateral circulation following adhesions around the liver "might be beneficial to the economy . . ." "(1) By somewhat diminishing the flow of blood through the liver it may enable that organ to deal more satisfactorily with the blood passing through it and so reduce the toxemia, which is probably the important factor in inducing ascites. (2) That the presence of vascular adhesions over the surface of the liver would relieve venous engorgement and so allow a freer supply of arterial blood to the liver. The nutrition of the liver cells would thus be improved and they would be under better condition to undergo compensatory hyperplasia. The compensatory hypertrophy of the liver will enable the organ to perform more efficiently its important antitoxic function, and so lead to a latency of the symptoms" (See Rolleston and Turner, Weber and Rolleston, references appended).

Late operation can only end disastrously. If the Talma-Morrison operation is to accomplish its purposes it must be performed before there is overpowering debility and advanced degeneration of the liver parenchyma. It can offer no advantages in the presence of deep jaundice or marked cardiovascular lesions.

Sinclair White's material collected by him includes 227 cases of cirrhosis operated, of which 37—or 13 per cent—were improved; in 15 per cent the operation failed, and in 33 death followed. The French

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(Monprofit) report the recovery of 35 per cent of 224 operated cases. Willems reported only 4 per cent of successes in 250 operated cases. Bunge in Germany presents in his work 288 operations, of which 70 per cent proved to be cirrhosis, with 30 per cent of cures and improvement in 14 per cent.

American physicians and surgeons have not become enthusiastic supporters of the operation; they interpret their results and those of foreign surgeons as rather discouraging. The efficacy of the operation cannot be fairly judged because in most cases it is postponed until the latest possible moment. It appears that the early operation does materially improve the chances of inducing latency of the disease and in some cases its complete arrest.

Duration of Laennec's Cirrhosis.—It is difficult to give any data of value which justify any conclusion concerning the duration of Laennec's cirrhosis. As already emphasized, early diagnosis is the exception; long periods of latency are frequent without subjective symptoms; compensatory changes often take place while the disease remains unnoticed. Years may lapse without progression after the positive diagnosis. There are *acute cases* which run a rapid course, particularly in young subjects. The duration of the average case depends largely upon secondary changes due to portal stasis and toxemia. There are but few chronic cases which die before the end of the second year following diagnosis. The majority live longer. The duration of cases detected early with good resistance depends upon the patient's ability to free himself from the slavery which holds him. *Limited liver changes of productive character may remain stationary, and because of compensation, such patients may for all practical purposes be considered cured.* Patients with mixed cirrhosis, with syphilitic liver lesions, and improvement following the intensive treatment with the iodids, may live many years and may die of other disease.

Experience teaches that but few patients die directly from cirrhosis; most deaths are due to secondary changes in distant organs or to complications—infection and toxemia—invited by the primary disease.

(*b*) *Unilobular Cirrhosis*

(*Hanot's Cirrhosis, Biliary Cirrhosis, Cirrhose Hypertrophique avec Ictere Chronique, Hypertrophic Biliary Cirrhosis, Obstructive Biliary Cirrhosis*)

General Statements.—Hypertrophic biliary cirrhosis and obstructive biliary cirrhosis are not exactly synonymous; both may be considered biliary cirrhosis but they differ from each other. In the former there is no gross obstruction in the larger bile duct, while in the latter (obstructive biliary cirrhosis) there is positive evidence of obstruction, to the out-

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flow of bile, which is followed by dilatation of the biliary ducts, destruction of liver cells, pigment deposit, and connective tissue proliferation. *Obstructive biliary cirrhosis* can be experimentally produced in animals by tying or obstructing the common duct. *Biliary cirrhosis of Hanot* is unilobular, involving one lobule of the liver tissue at a time; it may be complicated with true portal cirrhosis, and is characterized by marked *enlargement of the liver and spleen, jaundice which is persistent, febrile attacks* which recur, and the *absence of ascites* in uncomplicated cases. Men are more subject to the disease than women, and it shows a decided preference for young subjects (20 to 30 years—rarely after 40). The juvenile type of the disease is occasionally found, and this has been described by Gilbert and Fournier. Requin in 1846 was the first to mention the disease, Todd in 1857 again called attention to it, but Hayem in 1875 succeeded in giving a classic description of its clinical and pathological features, and Kiener in 1893 named it Hanot's disease.

Causes.—It is exceedingly difficult in the average case to give a cause for the far-reaching liver changes; neither alcohol nor syphilis account for the lesions. In the *obstructive biliary cirrhosis* the etiology is clearer, though pathologists are not entirely agreed; the fact remains that in a number of cases obstruction of the common duct by gall-stones or other pressure occurs. Rolleston assumes that when the symptoms of cirrhosis follow obstruction, "due to gall-stones or other causes, the cirrhosis is reasonably explained as the result of poisons manufactured in the intestines and carried to the liver by the portal vein." Naunyn says the association of gall-stones and biliary cirrhosis is rare but possible, and that gall-stones are secondary and not the cause of the biliary cirrhosis.

Complications.—*Attacks of pain in the region of the liver* with the physical changes mentioned and increase of the jaundice, sometimes acute enlargement of the already enlarged liver are depressing, and tend when associated with fever to weaken the patient and increase the tendency to myasthenia. Marked *change in the pancreas* is characteristic of some cases (See Chronic Pancreatitis) and interferes with digestion, and often proves a serious handicap—patients emaciate rapidly or they fall into a chronic condition of enfeeblement from which they do not lift themselves.

The renal and cardiovascular complications of portal cirrhosis may accompany the biliary type. *Purpura* (petechiae) has been noted in some of our cases, particularly with other toxic symptoms and has proved to be a difficult complication to treat; usually it is present in the terminal stage. *Nose-bleed* is at times profuse.

Hemorrhages from the intestine are rare, as are *hemoptysis, hematuria* and *hematemesis* save in the terminal stage, and then are not frequent. Gastrointestinal symptoms are often persistent. The *complete anorexia* in some cases with nausea, at times diarrhea, depleting the patient, lead to marked marasmus, cerebral anemia, mental confusion and death.

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Course of the Disease.—*The size of the spleen is variable.* Ordinarily the spleen is enlarged and palpable; in some cases the enlargement of the spleen is greater than the liver (splenomegaly), in other cases the liver is enlarged out of all proportion to the size of the spleen and it may happen that the spleen is miniature in size, in the presence of a good sized liver—or the liver in some forms of atrophic biliary cirrhosis may ultimately be small and the spleen enlarged.

Jaundice is a permanent feature, it may show variations in depth, and may be so deep as to give a brownish cast to the skin.

Joint changes do not materially influence prognosis; they are occasionally found. *Clubbing of the fingers* is evidence of advanced disease but slowly progressive. *Deep invasion of the nervous system* is always unfavorable. The *chronic cholemia* often causes mental hebetude and with depression there may be acute exacerbations of an emotional nature. Many cases terminate in a condition of profound *toxemia. Delirium* may persist during several weeks or days, *hiccough* with *delirium, convulsions* and *coma* are all possible; all are terminal.

With progression there is *myocardial insufficiency*—often *hemic* and *mitral systolic murmurs.* During the chronic stage the pulse continues reasurring without marked change in tension. As the end approaches or as the chronic toxemia begins to show its ravages, the pulse becomes more rapid, feeble and small; there are often symptoms of cardiac insufficiency and dilatation.

Blood.—The blood picture varies with the stage of the disease and associated conditions. In the plethoric adult polycythemia is not unusual. Emerson has reported counts as high as 7,800,000 and 8,500,000 in 2 of 5 cases; while the same writer reports the other extreme showing the usual characteristic *secondary anemia* of the disease—1,504,000. *Hemoglobin* may be increased in the individual cell or decreased, depending largely on the stage of the disease and complications. Moderate *leukocytosis* is the rule. Marked leukocytosis as in portal cirrhosis is not, as a rule, favorable.

Urine.—The quantity of urine in the average case is increased. Milian holds that *polyuria* is the rule and is characteristic. There are always evidences of jaundice (bile pigment) in the highly colored urine. *Urobilinuria* is frequent as is *indicanuria. Albuminuria* is less likely to be found with biliary than with portal cirrhosis. When present, its cause must be determined; it is often transitory. *Persistent albuminuria is unfavorable. A moderate shower of casts with jaundice is not of grave import; with albuminuria and casts and evidences in the heart and arteries as well as the nervous system of added* NEPHRITIS *the* PROGNOSIS *becomes more serious.*

Diabetes mellitus or *glucosuria* with hypertrophic cirrhosis is exceedingly rare. Sugar tolerance may be increased. *Incipient obstructive bil-*

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iary cirrhosis in which the cause may be removed surgically or yields to nature's processes, may remain stationary.

Conclusions.—*Hypertrophic cirrhosis of Hanot is an insidiously progressive disease which, as already indicated, finally causes overpowering toxemia and death.* The acute infections, gastro-intestinal complications, hemorrhage from the stomach or intestines, carcinoma, myocardial degeneration, nephritis, cerebral anemia, or meningitis, are among the most frequent causes of death. This variety of cirrhosis, as portal cirrhosis, invites *erysipelas, pneumonia* and *peritonitis.* The duration is from one to twelve years. One of my cases died in the twelfth month; the average of my cases has been two and a half years after positive symptoms. Goluboff reports cases of twelve years' duration. Rolleston gives the average as five years. *Much can be done to prolong life by proper attention to diet and to detail. Environment and habits are potent prognostic factors.* I know of no authentic cure.

In rare cases ascites may finally prove to be a terminal symptom; these are cases of the mixed type. Other individual symptoms not mentioned in connection with biliary cirrhosis, but fully considered in connection with portal cirrhosis, are of equal prognostic value in both varieties of the disease.

(c) *Pericellular or Syphilitic Cirrhosis*

Syphilitic cirrhosis is considered in the section on syphilis (See Syphilis of the Liver).

Unexpected disappearance of liver masses due to syphilitic cirrhosis and large tumor formations (gummata) follow antisyphilitic treatment very often. The enlarged or uneven livers of unknown origin given the benefit of antisyphilitic treatment are also frequently and favorably influenced. *Liver syphilis* is surprisingly frequent; under rigorous treatment, even with productive changes, it offers a fairly good prognosis. I have experienced so many successes that specific treatment is now commended in all cases of enlarged or nodular liver.

With *congenital syphilis pericellular cirrhosis* or *diffuse intralobular fibrosis* may develop. The clinical and pathologic picture of acute diffuse hepatitis may be present early with congenital syphilis, from which recovery is often possible and with which pericellular cirrhosis is finally closely related. Many of these children recover when the luetic character is recognized and leads to prompt and rigorous treatment. With jaundice, the prognosis is less favorable than without it.

(d) *Capsular Cirrhosis*
(*Perihepatitis*)

Associated Symptoms.—Perihepatitis is often of syphilitic origin, both in adult and in early life, and is associated with other liver changes due

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to the same cause. In these cases there may be proliferation of connective tissue sufficient to compress branches (large and small) of the portal vein causing *obstruction*, ascites, and the other usual symptoms. These cases are examples of *peripylephlebitis syphilitica*. *Jaundice* is present according to Leube in one-third of all cases and *enlarged spleen* is the rule. *Specific perihepatitis* may with advanced liver syphilis be associated with *amyloid degeneration of the liver*, and in some cases one or many *gummata* may be present in the organ. Fever and pain in the regions of the liver are characteristic, and are aggravated by pressure. The therapeutic test applied to cases in which amyloid change is not general or diffuse in the liver, proves the prognosis of many of these cases (usually with limited productive changes in the liver) to be relatively favorable (See also Syphilis of the Liver).

Chronic hyperplastic hepatitis (*Pick's disease, periserositis—Zuckergussleber*) is separately considered (See Periserositis in connection with pericarditis and peritonitis, etc.). These cases live for years with chronic obstructive symptoms and obliterating pericarditis, enormous capsular thickening of the liver and spleen with ascites. After years, during which these patients are tapped at short intervals, complications are likely to develop including the toxic state, marasmus, at times pneumonia or other infection; no case ever recovers.

Another class of cases includes besides the *chronic proliferative peritonitis, chronic perisplenitis* without any marked cirrhosis; but according to Hale White there is always *preceding chronic interstitial nephritis*. *Ascites* in these cases is a terminal complication; death usually follows before a second tapping is demanded.

Hale White found 14 of his cases demanding tapping. The average duration of life after the tapping was only 8 weeks. Of 10 cases which were tapped more than once the post mortem in 4 proved the diagnosis to be wrong. "Each of the other three had chronic peritonitis and perihepatitis; the remaining six had peritonitis, more or less chronic, associated with the cirrhosis."

Ascites with chronic perihepatitis is of extreme gravity. Fagge found "one fatal case of ascites from perihepatitis to every five fatal cases of ascites from cirrhosis."

Hale White offers statistics based on 22 cases of which number 14 had perisplenitis. He believes that perihepatitis and perisplenitis in this variety of the disease are a part of the general chronic peritonitis. In 19 of the 22 cases there was chronic interstitial nephritis. In 19 of the cases there were "evidences of failure of the heart or lungs and consequently sometimes the liver was *"nutmeg"*; in one case in which the cardiac failure was extreme there was jaundice, but this was the only instance of jaundice in perihepatitis." The average age of White's cases was 47½ years; the youngest was 29 and the oldest 68. There were 13 males and 8 females.

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Evidences of the fatal termination include ascites, general edema, increasing myasthenia, the toxic state, increasing heart weakness, the general features of amyloid disease and often cerebral manifestations.

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See references also—Peritonitis and Pericarditis.

5. Abscess of the Liver

(Suppurative Hepatitis, Tropical Abscess of the Liver, Suppurative Pylephlebitis)

General Considerations.—Abscess of the liver is either *single* or *multiple*. The single or solitary abscess is the more favorable for prognosis. *Tropical abscess* is usually single and is frequent among continental inhabitants in India after exposure to heat and alcohol excess, with infection. I have elsewhere considered the relation and prognosis of liver abscess to *amebic dysentery* (See Dysentery).

Small and hidden single abscess of the liver buried deeply in the substance of the organ offers a less favorable prognosis than does the large and superficial abscess. It is unusual for liver abscess to follow direct *trauma*, though this is possible.

The majority of all abscesses in the liver are due to infection through the blood stream or bile passages—hence they are secondary to distant or coincident disease. The portal vein is the usual avenue through which pus-producing germs enter. These include among others the *strepto-* and *staphylococcus*, the *pneumococcus* and the *coli commune*. I have else-

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where considered abscess due to *actinomycosis* and the infection of the liver following or associated with *amebic dysentery.*

The most frequent causes of liver abscess dependent upon hematogenous infection are appendicitis, dysentery, typhoid fever, tuberculosis, cancerous ulceration, pyogenic disease of the spleen and pancreas.

Infection through the bile passages causing liver abscess results from infectious cholangitis and cholecystitis; gall-stones are the most frequent cause. *Foreign bodies* including *worms* are also among the infecting possibilities. It is possible for suppuration within an encapsuled echinococcus to cause liver abscess (See Echinococcus Disease).

(*a*) *Single or Tropical Abscess*

Most tropical abscesses are secondary to dysentery (See Amebic Dysentery). Sodre's statistics (1907) show that in autopsies of dysenteric subjects 20 per cent had liver abscess. Kelch and Kiener found that in 314 cases of liver abscesses, 268—or 75 per cent—had dysentery.

Statistics bearing on the incidence of tropical abscess are not entirely reliable, as European subjects in India show a much larger percentage of liver abscess than do the natives, while the latter, when they contract dysentery, are more profoundly affected by the disease than are the former.

Rolleston reports 79,723 cases of dysentery among the natives, with but 127 liver abscesses—1 in 628; "while in the European army during four years (1893-96) there were 7,972 cases of dysentery and 441 cases of abscess, or 1 in 18."

Liver abscess in the tropics may be secondary to typhoid fever; occasionally influenzal infection is a cause. Malta fever, yellow fever, and erysipelas (streptococcus) infection are among the primary diseases. *Alcoholic excess* predisposes to liver abscess. It has been found that teetotalers are less likely to develop tropical abscess than are the native alcoholics; indeed abscess is rare in non-alcoholics (Rolleston). *Uncomplicated malaria* is not considered to be a cause of liver abscess.

Duration.—Tropical abscess may be present in the liver without giving rise to symptoms; hence it is impossible to be certain of its duration in many cases. When single abscesses rupture, either into the lung or into the alimentary tract, a fistulous opening may persist during long periods.

Spontaneous cure of abscess is an occasional occurrence. The abscess becomes encapsuled and "dries." Waring reported that in 25 cases which recovered, 2 "underwent spontaneous cure." The possibility of mistaking gummata for liver abscess, in some of these cases, must be considered. *Unrelieved tropical abscess* may lead to secondary abscesses in the lung; in other cases general pyemia may result. Most patients die of exhaustion with all of the constitutional symptoms of pyemia.

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Rupture.—*Neglected or undetected cases may rupture in one of many directions.* The frequency of rupture naturally depends upon the diagnosis as well as the treatment. Prompt surgical treatment reduces the percentage of ruptures. Most cases rupture upward and through the diaphragm. We quote Cyr's and Thierfelder's statistics as given by Rolleston:

Cyr—159 Cases		Thierfelder—170 Cases	
Lung	59	74	
Pleura	31	26	59 per cent.
Pericardium	1	4	
Periotoneum	39	23	
Stomach	8	13	
Intestines	13	32	
Kidney	2	1	
Inferior vena cava	3		
Bile passages	4		
External	2		

Complications.—Among the complications which may lead to death are abscess of the brain, purulent pleurisy and pericarditis, pneumonia, adhesions of the intestines causing obstruction, thrombosis of the inferior vena cava, and amyloid degeneration of the liver and other vital organs in the more chronic cases.

Blood.—The *blood count* is of greater diagnostic than prognostic value. *Leukocytosis* is the rule; there are exceptions, however, as was demonstrated by Osler.

Mortality.—Naturally the *prognosis of tropical or single abscess depends upon the early diagnosis and the result of timely surgical interference.* Solonoff collected 1,094 cases with a mortality of 30 per cent. This mortality is being reduced by improved surgical technic and greater diagnostic accuracy. Osler gives the mortality as 50 per cent.

Lafleur and Manson do not agree entirely in their conclusions. The former holds that the prognosis of amebic abscess is more unfavorable than other forms of liver abscess, while Manson has not had a similar experience. It may be concluded that the prognoses of single liver abscess is good in cases which are superficial and operated early. The prognosis of cases which rupture externally is also good. Internal rupture is less favorable, the course of such cases is often exceedingly chronic, and death from exhaustion and pyemia is to rule. Here too statistics differ.

DeCastro reports 76 per cent of recoveries after rupture into the lung; others offer much lower figures: Manson 50 per cent, Lafleur considers the prognosis of the complications unfavorable. Rupture into the intestine offers a favorable forecast.

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Course of the Disease.—*Rupture into the peritoneal cavity* is promptly followed by general peritonitis and death. *Amebic abscess in the presence of an active and persisting dysentery offers an unfavorable prognosis.*

Single liver abscess may cause multiple deposit in the organ finally; these cases are always fatal. With chronic abscess, increasing anemia, albuminuria, circulatory weakness and obstruction (edema), intestinal symptoms, invasion of the sensorium, and amyloid disease are of the gravest import.

(*b*) *Multiple Abscesses of the Liver*

(*Suppurative Pylephlebitis, Pyemic Abscesses of the Liver, Portal Pyemia*)

Causes.—Whether multiple abscesses of the liver are due to infection through the hepatic artery or portal vein, to suppurative cholangitis, or to the single tropical abscess, the prognosis is bad and death is the rule. Most multiple liver abscesses are due to *gastro-intestinal lesions.*

Appendicitis is unquestionably the most frequent cause of purulent pylephlebitis. The incidence of suppurative pylephlebitis with appendicitis is only 0.5 per cent.

Langdon Brown collected 64 cases of suppurative pylephlebitis of which 27 were due to appendicitis—42.2 per cent. Fitz found 11 cases in 257 of perforative appendicitis. Kelly and Hurdon report 10 with pylephlebitis among 86 fatal cases. Gerster found only 9 cases among 1,189 operated at Mt. Sinai—0.75 per cent.

Among the other causes of multiple abscesses of the liver are gastric and duodenal ulcer, cancer of the stomach and intestines, infection following foreign bodies, pelvic infection, rectal fistula and carcinoma, infected hemorrhoids, gall-stone disease with cholangitis, infected spleen and pancreas and as already mentioned (See Tropical Abscess) *single liver abscess may cause portal pyemia* (multiple abscesses).

Course of the Disease.—The clinical history is synonymous with septicemia and pyemia. Death is preceded by a limited period which includes repeated chills, intermittent fever, abdominal pain and distention. As the disease progresses the nervous system is profoundly affected, and death in coma is the rule. Langdon Brown gives the average duration forty-seven days. There may be a much shorter or longer duration, varying, as we conclude from our own reported cases, from 3 to over 200 days. In all cases there is first the history of the underlying disease, second, the development of the septic state, and third, the evidences of liver abscesses (Taylor).

Accompanying Symptoms.—*Jaundice* is not a symptom of prognostic value. It may or may not be present. *Liver enlargement* characterizes most cases. *Splenic enlargement* may be expected in about 20 per cent

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of cases. *Hiccough* is an annoying and persistent symptom when present —often uncontrollable.

Secondary anemia and leukocytosis are usual (10,000 to 28,000). Libman reports 15 cases in which he cultured the blood with negative results in 14. In the one case which was consecutive to calculous cholangitis pneumococcus infection was present. I know of no well-authenticated case of recovery. Once the portal vein and its branches are included in a pyemic process, death is certain to follow. In those cases which are reported as having recovered, the correctness of the diagnosis may be doubted. Rolleston says: "Conceivably this verdict may require some modification in the light of more frequent observations of the state of the liver as seen in the course of exploratory laparotomies. In isolated cases recovery has occurred in which multiple abscesses were thought to exist, but some question must arise if suppurative inflammation of the portal vein was present." Evidences of healed suppurative pylephlebitis were found in cases reported by Goodhart and Moschowitz.

Quenn and Mathieu report 13 cases which recovered after operation, all due to appendicitis. Treves and West have recorded two cases.

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6. Neoplasms of the Liver—Cancer of the Liver

General Statements.—Cancer of the liver should always make the clinician suspicious of a primary growth in another organ, and search should be made in all directions to determine the location of such growth. The diagnosis of primary cancer of the liver should always be omitted until confirmed post mortem.

Hale White found in 18,500 autopsies at Guy's Hospital 24 cases of *primary cancer* of the liver (0.13 per cent.). Eggel places the percentage at 0.05. Rolleston places the numerical relation of primary and secondary cancer of the liver between 1 to 20 and 1 to 40. Hale White, 1 to 21—Hansemann, 1 to 40.

The majority of liver cancers are epitheliomata of the cylindrical variety or medullary; *sarcoma of the liver* is exceedingly rare, either as a primary or secondary disease. *Melanosarcoma* is a frequent form of sarcoma of the liver. When it attacks that organ it may be secondary to choroidal growths or melanotic degeneration of pigmented skin (Jacobi).

Secondary cancer of the liver is, as a rule, multiple. The organ is enlarged, the nodules are usually scattered throughout the organ, there may be but one nodule; occasionally there is diffuse carcinomatous infiltration. The liver is large, the nodules are prominent and umbilicated, the edge of the liver is irregular and nodular, the gall-bladder is often distended, may also be carcinomatous, and may contain gall-stones. The portal current carries the disease to the liver from either the stomach, intestine, esophagus, pancreas, or the growth may come from some other unsuspected organ, as the prostate, uterus, kidney and rectum, or occasionally it happens that there is direct extension of the growth from one of the neighboring organs. In doubtful cases the stomach is the most likely primary source of the disease often there are also metastases to the supraclavicular glands.

Primary cancer of the liver may be either diffuse or there may be but a good sized nodule. The large nodule may ultimately be surrounded by few smaller growths; there are often glandular infiltrations in the hilus *without distant metastases.*

Factors Which Influence Prognosis.—*Jaundice.*—With persistent jaundice of unknown cause, which remains uninfluenced by treatment, usually accompanied by progressive loss of weight, cancer of the liver should be suspected and prognosis accordingly given. Jaundice is present in 50 per cent of all cases. Deep jaundice is indicative of obstruction by cancer nodules of the hepatic or common ducts. Jaundice is rare with primary cancer of the liver.

Edema of the extremities is a terminal symptom. *Thrombosis of the femoral or saphenous veins* may be responsible for edema of the left leg and is usually a late complication.

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Ascites is less marked than in alcoholic cirrhosis; the fluid is likely to be bloody; ascites is present in most cases and is a late complication—it is usually associated with far-reaching infiltration, cachexia, and heart weakness. Life is not prolonged after its appearance for any considerable period. Diffuse cancerous peritonitis may be the cause of ascites in some of these cases. While the *fluid,* as already stated, may be bloody, it may be clear or cloudy or bile-tinged in some cases; the clear or cloudy fluid may later become bloody.

Spleen.—With uneven liver and suspected carcinoma, the presence of an enlarged spleen argues against cancer, for the spleen is rarely enlarged in liver cancer. There are but few exceptions.

Fever is usually a late symptom and may be due to toxemia, or in occasional cases to associated cholangitis.

Mortality.—The prognosis of cancer of the liver is absolutely bad. Surgical treatment offers nothing for secondary or multiple liver cancer. There are references in medical literature to supposed successful excisions of a part of the liver, where the disease was primary, detected early and limited to a constricted lobe. Some success has been claimed to follow the removal of the cancerous gall-bladder and adjacent infiltrated liver tissue. Keen's statistics include 76 cases of liver tumor of which 63 recovered, but of the 76, 18 were carcinoma and 5 sarcoma. Neither the operations for carcinomata nor sarcomata when thoroughly analyzed offer much that is encouraging.

Mayo Robson's case—in which a small secondary liver nodule was removed at the time of the resection of the primary stomach cancer—is reported to have recovered.

Practically all liver carcinomata operated have been followed by recurrence and multiple deposit; indeed it may be assumed that in most of these there was already dissemination at the time of the operation. Rolleston says: "But even in these cases, which can hardly be diagnosed with any certainy before the abdomen is opened, the disease usually returns and kills the patients. Operation for removal of malignant growths from the liver, whether from its substance or when starting in the gall-bladder, is the only means at one's disposal at present of mitigating the otherwise fatal prognosis."

Spontaneous Recovery.—It is true that occasionally cases of liver tumor diagnosticated as malignant have recovered spontaneously. The majority of these cases were specific and not malignant. The experiences, however, of reliable observers, who report cases of spontaneous recovery which they insist were malignant and cancerous, including Greig Smith, Gould, and Hopendyl, cannot be entirely ignored.

But few cases live beyond twelve months and most die in a much shorter time. As a rule, the course of the disease is comparatively rapid, and death may follow within from three to six months after the diagnosis

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has been made. *Encephaloid cancer of the liver* usually grows with surprising rapidity. In one of my cases the growth almost filled the abdomen in less than five weeks and caused death by rupture with consecutive sudden hemorrhage into the peritoneal cavity. A rent in medullary growths has suddenly ended the lives of a number of cases.

Hale White holds that the *course of primary cancer of the liver is practically acute,* and life is rarely prolonged beyond four months. Latency is possible; death may follow a short period of activity. Exceptional cases covering long periods are recorded. Christian had one case in which liver cancer was secondary to a rectal growth in which the liver was enormously enlarged for thirty-five months before death, and Taylor reports a case which lived three years. Increasing weakness and toxemia including final coma during several days end most lives. There is always with cancer of the liver the hope that the diagnosis is wrong and that the nodules may prove to be specific gummata or other benign growths as hydatids or angioma.

Heredity.—My statistics showed heredity in from 15 to 20 per cent of all cases. The sexes were almost equally afflicted with the preference favoring men with primary cancer, and women with secondary disease. The average age was between 40 and 60 years.

I have seen several primary sarcomata of the liver in early life and have records of one congenital case. Rolleston collected 32 cases of primary sarcoma of the liver under 10 years of age. Picot in 424 cases of malignant disease under 17 years of age found 13 of primary malignant disease of the liver. Noeggerath and Jacobi each report a case of congenital liver malignancy.

General Conclusions.—*Sarcoma of the liver* offers an unfavorable prognosis; as already stated, it is rarely met.

Benign growths of the liver include *fibroma, angioma* and *cysts.* Liver cysts and cystic degeneration of the kidney are almost always coincident (Bristowe). Many of these are operable and favorable. I have separately considered the *leukemic infiltration of the liver* (See Leukemia).

Multiple adenomata of the liver are, as a rule, found with cirrhosis. In these cases there is usually ascites and hematemesis, portal thrombosis, and advanced asthenia. The prognosis under such conditions is naturally bad.

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7. Fatty Liver

Fatty infiltration and *fatty degeneration* of the liver are secondary processes.

Fatty Infiltration.—Fatty infiltration may be physiological. It is not unusual to have an excessive accumulation of fat in the liver in young children. It has been found in normal pregnant women who die accidentally, and in the obese.

Fatty Degeneration—Fatty Liver.—The liver is uniformly and evenly enlarged, rather soft, the border is smooth and rounded, there is no jaundice neither is there pain nor enlarged spleen. *Advanced fatty degeneration of the liver in chronic alcoholics is common.* It may accompany cirrhosis and it is unfavorable under such conditions. It may result from *acute* or *chronic poisoning* among which *phosphorus* is most prominent. The other poisons which may cause fatty degeneration are arsenic, antimony, copper, chloroform and the various acids.

Fatty liver is frequent with infectious diseases, dependent upon the destructive influence of the toxins (typhoid fever, pneumonia, puerperal fever, smallpox, diphtheria, scarlet fever, cholera, erysipelas, and the other malignant infections. (Roger and Garnier, also Rolleston.)

In connection with appendicitis, I mentioned the danger of acute *fatty degeneration of the liver with appendicitis.* It is sometimes in such cases difficult, when death follows operation to determine whether the liver destruction is due to the anesthetic or to the infection. Such a case I recently saw in Frankfort, Germany. The death of the boy aged 14 years followed within three or four days after appendectomy; the liver was found with universal fatty degeneration.

Fatty degeneration and enlargement of the liver with pernicious anemia is a late manifestation of the primary and progressive disease. With *cancer, tuberculosis, chronic respiratory and heart lesions,* the prognosis of fatty liver must of necessity be that of the primary disease. It has been observed that *alcoholics with fatty livers bear infection and surgical interference badly*—they develop toxemia and cardiac asthenia on slight cause.

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Acidosis is very likely to follow any operation of importance; even slight insult is badly borne.

Pneumonia is a frequent cause of death.

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8. Amyloid Liver

(Waxy Liver, Lardaceous Liver, Chondroid (Wells) Liver)

General Statements.—*Amyloid degeneration of the liver is always secondary and when advanced is associated with progressive and fatal disease.* The diseases which usually precede waxy change in the liver are chronic *tuberculosis, syphilis, prolonged suppuration,* and *chronic bone disease.* The degeneration shows its earliest changes within the arterial zone of the hepatic lobules; the minute vessels—arteries, capillaries—are involved. The degenerative changes in the vessels extend to the central and peripheral vessels. The liver is enormously increased in size, is hard, its surface is even, its border rounded, there is no jaundice, but anemia and ascites are present; the enlargement is painless, and the spleen is enlarged.

Amyloid degeneration in other organs—the spleen, kidney, gall-bladder, and the glands in the portal fissure—is common. With advanced waxy liver, the anemia of the patient, his color and general dropsy are characteristic. The experienced clinician recognizes these features of the disease which forecast early death. Albuminuria is a constant attendant of advanced lardaceous disease.

Limited amyloid changes in the liver, without marked enlargement with acquired or congenital syphilis, radically treated, may recover.

Limited amyloid changes of syphilitic origin with cirrhosis, not far advanced, are amenable to intensive treatment. Amyloid degeneration with the essential anemias—leukemia particularly—has been found a terminal complication in my experience.

I have never failed to find evidences of widespread amyloid degeneration, post mortem, in other organs besides the liver; it is this fact which makes the prognosis bad besides the usually fatal primary disease. In practice it will be found that enlarged livers which are diagnosticated as *waxy,* which recede under treatment are positively syphilitic. I have never known of recovery from a supposedly amyloid liver in which the diagnosis of syphilis was not justified and the therapeutic test was not convincing.

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9. Echinococcus of the Liver

See Section I—D (Internal Parasites).

10. Syphilis of the Liver

See Section I (Syphilis).

11. Tuberculosis of the Liver

See Section I (Tuberculosis).

K. Diseases of the Bile Passages and the Gall-Bladder

1. Acute Cholangitis

(*Acute Catarrh of the Bile Passages, Acute Duodenocholangitis*) (See Catarrhal Jaundice)

When acute cholangitis is a part of a general infection, secondary to some one of many infectious diseases, it ends an element of danger, but the prognosis always depends upon the malignancy and nature of the primary infection. *Infection of the common duct and gall-bladder with typhoid fever, pneumonia, or other diseases may lead to chronic changes and is often responsible for subsequent gall-stone disease* (See Cholelithiasis).

2. Chronic Cholangitis

In rare cases an acute inflammation of the bile passages persists and becomes chronic. I have seen such cases in which several months of jaundice, uninfluenced by treatment, created the suspicion of serious organic (malignant) disease; the obstruction finally yielded and there was full recovery. In such cases there may be suggestive loss of weight, but the other serious manifestations of grave icterus are absent, including ascites, hemorrhage, petechiae, mental torpor and cachexia.

Chronic cholangitis is a frequent complication of liver cancer and cancer of the bile passages, and as elsewhere suggested, may under such conditions be somewhat influenced by treatment; but in the majority of cases the icterus of malignant disease, abscess of the liver, hydatids or other organic changes is due to mechanical pressure mainly, is persistent, and remains unchanged to the end.

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Gall-stones are provocative of chronic cholangitis by occlusion and infection; they continue symptoms until relieved either by nature's processes or surgical interference. In these cases there is likely to be associated *chronic pancreatitis* of the productive type (*chronic interstitial or fibroid pancreatitis*). With persisting obstruction, the liver substance may undergo organic changes, the organ enlarges, and chronic invalidism with great loss of weight results.

When there is persisting *complete obstruction of the common duct* or of the larger ducts, dilatation of the bile passages follows and jaundice remains. *Occlusion of the common duct* may be due to one of many causes and may be either complete or incomplete. Gall-stones are a frequent cause of such occlusion. Pressure from growths in the liver or surrounding organs, ulcerative processes of the duodenum at the ampulla of Vater, or in the duct itself, with final cicatricial contraction have been found in my cases. Surgical interference in non-malignant cases offers a favorable forecast.

3. Suppurative Cholangitis

Suppurative cholangitis is always secondary; usually impacted gall-stones with infection are responsible; abscess of the liver (pylephlebitis), pyemia, erysipelas, puerperal infection, pneumococcus or influenzal infection, dysentery, and many other infections are causative. The condition is always serious; when far-reaching, is usually fatal. There is danger of *perforation*. The *gall-bladder* is often involved and filled with pus; there may be *multiple small abscesses of the liver and enlarged spleen*. The symptoms are those of deep infection, pyemia with *intermittent fever*, and in occasional cases there are associated metastases in other organs. The *parotid gland* is occasionally involved in *metastatic parotitis*. With multiple metastases the prognosis is always bad. Naturally the prognosis must depend upon the ability to remove the primary focus and drain the infected and suppurating area. The duration of suppurative cholangitis in fatal cases may be only a few days.

4. Acute Inflammation of the Gall-bladder

Cholecystitis

Acute infection of the gall bladder may be due to gall-stones, or it may depend upon direct infection of the organ with or without the invasion of other organs. The majority of cases are associated with cholelithiasis. The gravity of the disease depends upon the character of the infection and the depth of the gall-bladder change.

Uncomplicated acute catarrhal cholecystitis is rarely diagnosticated, and leads to recovery without leaving a remnant.

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5. Chronic Cholecystitis

With *gall-stones* in the gall-bladder, catarrhal changes may lead to *chronic cholecystitis,* thickening, increase of mucus in the gall-bladder, and all without symptoms, or there may be an indefinite train of symptoms which suggest mild infection—all of which disappear with the drainage of the gall-bladder. If untreated, constitutional disturbances gradually develop, due to general infection and toxemia with loss of strength, fever, and kidney involvement; death may result. Once diagnosticated or suspected in the absence of complications with modern radical treatment, recovery is the rule. *Chronic cholecystitis* leads to dilatation of the gall-bladder besides the changes already mentioned; with pyemic infection, to *empyema of the gall-bladder.*

Hydrops, or dropsy of the gall-bladder is also the result of cholecystitis. The prognosis of empyema and hydrops of the gall-bladder is good with drainage in most cases.

Infections of the gall-bladder leading to empyema may result from cholangitis, but gall-stones are the most frequent cause.

6. Obliterative Cholecystitis and Cholangitis

Any organic disease of the bile passages which causes ulceration or productive change or pressure which is sufficient, may cause occlusion with consecutive changes and chronic jaundice.

Duodenal ulcers may involve the ampulla, and cause stricture of the common duct; gall-stones in their passage or by ulceration may in the process of healing lead to stricture or complete occlusion.

Following the ulceration of gall-stones into the intestine or surrounding organs, adhesions often form which occlude the bile passage and the surrounding viscerae may be bound to each other.

With partial obstruction of either the gall-bladder or larger duct, repeated attacks of pain may simulate gall-stone colic; fever, loss of strength and flesh with jaundice persist until surgery comes to the rescue.

Obliterating cholangitis of the common or hepatic ducts in which there is complete obstruction leads to permanent jaundice, which can be overcome only by surgical intervention. Without complication, the prognosis of this condition is relatively favorable.

Unrelieved obstruction of the bile passages leads to enlargement and chronic liver changes, weakening intermittent fever, jaundice, and death.

The prognosis of obstruction of the bile passages dependent upon conditions other than gall-stones or cicatricial contraction following ulceration, is not good because the responsible lesions in the liver or in the surrounding organs are usually malignant or exceedingly grave.

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Congenital obliteration of the bile ducts is considered in the chapter on icterus neonatorum.

7. Gangrene and Phlegmonous Cholecystitis

Gangrene of the gall-bladder is rarely found without gall-stones. With biliary colic, associated septic fever, and persisting local symptoms, cholecystitis should be suspected. Radical surgical treatment early, will save the majority with phlegmonous or gangrenous gall-bladder. My material includes patients beyond the age of seventy who were successfully operated without subsequent symptoms.

Acute phlegmonous cholecystitis with the infections, typhoid fever, pneumonia, or septicemia is exceedingly grave, most of these patients die.

Perforation of the gall-bladder is always a grave complication, and leads to peritonitis and death unless operated immediately.

Phlegmonous cholecystitis is a more common complication than has been heretofore supposed, as is demonstrated by the operative statistics of Mayo Robson and others.

8. Cancer of the Gall-bladder

Cancer of the gall bladder is not frequent and when found is usually secondary. The most frequent cause is the long continued irritation of gall-stones or extension from the neighboring organs. Futterer collected 248 cases of gall-bladder cancer. There are, according to Mayo Robson, only 10 cases of sarcoma on record. Mayo Robson found gall-stones in 73.2 per cent of his cases of cancer of the gall-bladder and bile ducts. Zenker found gall-stones in 85 per cent, Musser in 69 per cent, and Courvoisier in 88 per cent.

Early removal of the gall-bladder offers the only hope. When limited, the prognosis with early operation offers great encouragement; the results of surgeons who have had a large experience justify this conclusion. Authentic cases are recorded by Mayo Robson, Kehr, and others in which patients were alive and well years after cholecystectomy.

With metastases or when secondary to neighboring growths, the prognosis is absolutely bad.

The metastases are larger, as a rule, than the primary growth; the growths when primary in the gall-bladder are surprisingly small.

Primary cancer is occasional in the bile passages, usually in the opening of the common duct.

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9. Cholelithiasis

(*Gall-stones, Hepatic Calculus, Biliary Calculus*)

General Considerations.—The vagaries of gall-stones are numerous; the clinical history proves this and establishes the further fact that one or more gall-stones may often be tolerated in the gall-bladder or bile passages during unlimited periods without creating a suspicion of their presence and without causing secondary changes, and that the same gall-stones without the slightest warning may suddenly cause life-threatening complications. There is no other condition associated with disease of the digestive system in which such a variety of clinical pictures may be presented; none in which tolerance to an anomaly is longer borne; none in which the danger may arise more suddenly; none which may so promptly change from an apparently benign to a serious disease; none which may so insidiously produce organic changes in the organ which holds it, including the liver substance as well; none in which distant and constitutional changes and infection may prove more damaging; and none which offers so many interesting features for study as does cholelithiasis. In the consideration of the conditions which lead to the formation of gall-stones, we are practically agreed that infection is a *sine qua non,* whatever theory we adopt.

Naunyn holds that cholesterin, the main constituent of gall-stones, is not a product of metabolism nor a specific secretion of the liver cell, but that it is found in the secretion of all inflamed or infected mucous membranes. In cholelithiasis, he contends, it originates not in the bile but in the mucous membranes of the bile passages and the destroyed or broken down epithelia. The normal cholesterin content of the bile is made innocuous by the protoplasmic poison which it holds. The lime salts are held to be of similar origin. Without primary change in the mucosa and its infection, these substances are not aggregated and gall-stones are never formed. Aschoff and Backmeister represent a new school. They hold that cholesterin is precipitated from the bile itself; that it is not necessary to have inflammatory changes of the mucosa of the gall-bladder or any mucous surface in order to form the stone; but that obstruction to the outflow of bile is sufficient. Further they hold that cholesterin may be precipi-

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tated in the presence of aseptic conditions, and that inflammatory change is unnecessary. The process is dependent upon a change in the concentration of the separate bile constituents, upon an increase of cholesterin concentration, and a reduction in solubility and resorption. Pure cholesterin stones may be formed in this way. Most authorities agree that *fixed stones are unquestionably dependent upon associated infection.* With infection there is (1) *stasis of the bile;* (2) *precipitation of cholesterin;* (3) *cleavage of albumin content,* and (4) *epithelial degeneration.* In pregnant women who are particularly prone to the formation of gall-stones, Hofbauer has demonstrated the presence of all of these conditions.

Women are more frequently afflicted than men, the proportion being 4 to 1. Naunyn found that 90 per cent of women with gall-stones have had children. The favorite age is between 40 and 50; infants and the newborn are occasionally found with gall-stones.

The *association of gall-stones with metabolic faults* is said to be frequent. *Diabetes, gout, and rheumatoid arthritis* are among these, but statistics concerning diabetics recently collected are not absolutely convincing.

With malignant disease the occurrence is strikingly frequent. The search made by gynecologists at the time of abdominal operations unearthed the presence of a large number of gall-stones with other conditions in which there are often disturbances of the internal secretions.

My material proves gall-stones to be present in 2.5 per cent of all internal diseases. Ten per cent of all autopsied bodies show gall-stones, and of this number 95 per cent never had symptoms which suggested their presence. My experience justifies the conclusion that *gall-stones while they give rise to no symptoms in many cases, are never to be considered harmless.* The prognosis is always materially influenced in those who are predisposed to metabolic faults by sedentary habits or any condition which leads to stagnation, also such diseases as prevent sufficient exercise—as chronic heart disease. The deposition of cholesterin is increased by lack of muscular movement.

Diet is also an important factor in the formation of gall-stones. The bile requires the presence of its normal solvents, sodium glycochocolate and taurocholate, which are provided by the nitrogenous foods in the process of metabolism. The absence of nitrogenous food encourages the precipitation of cholesterin. Mayo Robson says: "This may serve to explain the presence of gall-stones in gouty persons who on account of the lithic diathesis limit their intake of nitrogen."

Gall-stones, once formed, are not likely to dissolve spontaneously; neither have we any remedy which dissolves them in the gall-bladder or in the liver. Aschoff and Backmeister question the possibility of their solution; if possible at all, it is exceedingly rare. Naunyn contends that spontaneous solution is hardly probable, and that for cure we are never to depend upon such a possibility.

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Hanseman has recently apparently proved by experiment *in vitro*, and by transferring gall-stones from human beings to dogs, that gall-stones are soluble in normal bile, particularly stones composed largely of cholesterin. Hanseman's contentions hold that if the catarrhal conditions of the bile passages can be cured, inflammatory products removed, and the bile restored to its normal condition, the stones will be dissolved spontaneously—"normal bile under normal conditions does not permit concrement to develop and will dissolve in time those already formed. He further holds that the peculiar shape of the gall-stones found at the operation in many cases is due to their being partly dissolved." In practice we cannot subscribe to Hanseman's conclusions. It would be exceedingly difficult to obtain normal conditions of the bile passages and the bile, which he considers necessary in the presence of gall-stones.

I consider the prognosis of the

(a) *Acute biliary colic*
(b) *Chronic cholelithiasis*
(c) *Obstruction of the common duct*
(d) *Obstruction of the cystic duct*
(e) *Obstruction of the hepatic duct and intrahepatic ducts*
(f) *Complications and remote results.*

(a) Acute Biliary Colic

In patients otherwise normal, the gall-stone colic, while painful and depressing is well borne; the shock in most cases is not severe; the heart function remains uninfluenced and without remnant; recovery from the colic is complete after a few days of hypogastric and epigastric tenderness, associated fatigue, and anorexia.

I have had but one *death during the acute attack*—a woman nearly seventy years of age, with myocardial degeneration. This patient had a solitary stone, and she died of rupture of the heart, within one-half hour after the onset of the colic. Courvoisier has collected 41 deaths during acute biliary colic, and Naunyn 9 cases. *Collapse* is at times profound but the majority of patients react with the relief of pain.

Associated Symptoms.—With a *weak myocardium* and recurring colic at short intervals, death may result during the acute attack. *Perforation* may occur during the attack, may cause sudden death, or may promptly lead to peritonitis. *Relative mitral insufficiency* is not infrequent during acute exacerbation and colic. Riesman has called attention to this complication and I have found it present in a number of cases. With relief of the colic, usually within 24 hours, often sooner, if a true relative insufficiency, the murmur disappears. Riesman reports 56 cases of chlolelithiasis, 6 of which had a mitral systolic murmur.

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In weakened subjects an acute gall-stone colic may be followed by several days of depression, rapid pulse, and unsettled digestion.

The tender epigastrium and right hypochondrium are not followed by general tenderness or extensive peritonitis. It may however be safely assumed that *with each gall-stone colic there is more or less local inflammation which causes adhesions; consequently each exacerbation increases these inflammatory changes.* With repeated gall-stone colic the local changes, including thickening and adhesions increase, and unless the stones are removed, such lesions may sooner or later cause traction, pressure, obstruction, or other changes in accordance with the extent and location of the stone.

The *initial attack is usually the most severe,* for with repeated attacks the gall-bladder loses its elasticity, and the expulsive efforts are consequently more feeble; the duration is shorter, and with increasing adhesions, the pains and other symptoms of the colic are less severe and therefore more easily borne.

Jaundice is not always to be expected. There may be early or late jaundice depending upon the location of the stone and secondary changes. Less than one-third of all patients with biliary colic are jaundiced. Jaundice never develops when gall-stones remain in the gall-bladder or cystic ducts, but when during the acute colic the stone is held in the common duct, obstruction to the outflow of bile immediately follows with jaundice. Such jaundice persists until the stone is removed either by nature's process or by surgery.

Ball valve action of stones in the common duct may cause gall-stone colic with *intermittent jaundice—often with fever.* The persistence of jaundice after colic positively dependent upon gall-stones is a prognostic sign of great significance for it is positive proof of obstruction, usually in the common duct, though obstruction of the hepatic ducts, one or both, may also lead to jaundice.

Jaundice due to occlusion of the common duct by gall-stones may be present without colic. In such cases a stone of small size may find its way into the duct, be caught there, grow by aggregation until the occlusion is complete.

Fever is not always a symptom of great prognostic value with gall-stone colic. It is very likely to follow a well-defined early chill. *Hyperpyrexia with gall-stone colic* is as a rule evidence of *purulent cholecystitis,* cholangitis, or it may be an expression of hysteria or idiosyncrasy.

When, following a classic colic, *intermittent fever* persists after 24 or 48 hours, *empyema of the gall-bladder or purulent cholangitis* should be suspected.

The intermittent hepatic fever of Charcot—"intermittent biliary fever"—is due to the associated infection and the irritation of the mucosa by the stone. Kehr has found that the most frequent cause of intermittent

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fever is the impaction of the gall-stone in the common duct. When there are repeated acute attacks with intermittent fever, or if after one or more attacks, the fever continues to observe a characteristic periodicity, the stone is usually impacted or complication due to infection—ulceration, abscess, suppurative cholangitis, destructive cholecystitis, or other lesions are the cause and these are but rarely overcome without surgical intervention.

Vomiting.—Vomiting during the attack may have a salutary effect, for not infrequently the colic ceases when the stomach, which may be overloaded or still holds remnants of a previous meal, is unloaded. Vomiting or attempts to empty the stomach with but little or no food, may because of the pain added by the effort, increase collapse; perforation during vomiting has been reported but is a rare complication. When the vomitus contains bile, the common duct is not completely occluded.

Enlargement of the liver may be demonstrated during some acute attacks—by no means the majority. The palpable liver is tender, the symptom is not of serious import, and disappears after a few days. When present it outlasts the pain by several days. *The more severe the attacks the more likely is the liver to be enlarged.* The liver is usually tender to pressure because of the peritoneal irritation without evident enlargement.

Marked acute enlargement of the liver with acute biliary colic is not of serious significance. The rule is that such enlargement disappears promptly but recurs with subsequent attacks.

Enlargement of the gall-bladder during the attack may or may not be evident. During severe attacks the abdominal wall is so tense and tender that deep palpation is impossible. It is often possible to demonstrate the enlarged organ by directing the patient to take a deep breath, holding it long enough to percuss gently over the liver and gall-bladder, marking the outlines and comparing these with the result of percussion during the normal respiratory movement. In thin subjects this may not be necessary; gentle palpation may suffice. *With repeated acute attacks the possibility of adhesions must be considered.* The enlargement is likely to disappear suddenly and, without evidences of persisting acute infection, does not add to the dangers of cholelithiasis.

Slight enlargement of the spleen is common, but of no prognostic influence. The *urine* may be almost completely suppressed during a severe colic; as a rule, it is concentrated and materially reduced in quantity. Its color depends largely upon the degree of obstruction. The presence of albumin and an occasional hyaline cast are usual and not serious; the same is true of *transitory glycosuria.*

The *severity of the colic* is not in proportion to the size of the stone, but depends more upon the extent and depth of the inflammation. Small calculi often provoke greater local changes than do the larger. There is no rule.

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Rolleston holds "The prognosis in some degree depends on the presence or absence of facets on a calculus found in the stools. If, after a first attack, a smooth gall-stone without facets is found in the feces, it may reasonably be hoped that no further attack will follow. If, on the other hand, the calculus is faceted, there are more calculi in the gall-bladder and the probability of fresh attacks must be faced."

It is possible for small stones to find their way from the hepatic and cystic ducts through the common duct into the intestine. The size of the stone which may be passed directly through these passages varies in the individual cases, but it is rarely larger than a hazel nut, according to the experience of most clinicians (Grube and Graff). *When larger stones during acute attacks or at any time enter the intestines or are found in anomalous locations it is the result of ulceration and protective adhesions.*

The Blood.—With acute attacks and intermittent fever the blood has been found contaminated; Netter found Staphylococcus pyogenes aureus, and Sittman, Gilbert and Girode demonstrated staphylococci also. *The frequency of typhoid infection is striking and is of enormous etiologic and prognostic value.*

Leukocytosis with fever and gall-stone colic as a diagnostic and prognostic feature is of but little value, for it is not constant. Pick claims that the intermittent fever of gall-stone colic is always due to a purulent infection in which he claims the presence of leukocytosis, while Grawitz and others have failed to confirm his observations. My experience seems to justify the conclusion that with gall-stone colic and *persisting leukocytosis*, there is as a rule complicating infection, usually cholecystitis or cholangitis, or both; with a high leukocytosis and repeated chills and intermittent fever, suppurative cholangitis should be suspected or empyema of the gall-bladder.

X-Ray Examination.—I have failed to receive aid in the diagnosis or prognosis of gall-stones from x-ray examination. The shadow can only be present when the stone contains considerable lime. Negative results are valueless, positive results are rare. X-ray examination can but rarely be relied upon.

(b) Chronic Cholelithiasis

The presence of gall-stones in the bile passages during long periods *without biliary colic* or only *occasional acute exacerbation* is possible. In the majority of these there are insidious changes in the tissues which surround the stone, without marked symptoms. *A large proportion of such patients are chronic invalids; they may never appear very sick, neither do they ever feel perfectly well.* Over one-half of all gall-stones are in the bladder (55.5 per cent); 12.5 per cent in the gall-bladder and cystic

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duct; 10.5 per cent in the gall-bladder and common duct; 6.6 per cent in the common duct alone, and 6 per cent in the cystic duct alone (Kelly).

The prognosis of chronic cholelithiasis depends entirely upon added infection, mechanical influences, and secondary changes. *Chronic cholelithiasis is in the overwhelming number of cases a latent condition;* this simply means that subjective and objective symptoms may be absent during long periods, but does not preclude the possibility of local changes, which in the end may add to the dangers or may prove conservative, with or without complications.

Adhesions.—Cases of chronic cholelithiasis which during life may give but few or no symptoms are often found on postmortem to have caused extensive *adhesions.* In a proportion of cases *adhesions prove protective and prepare the way for the safe delivery of the stones into the intestines or other organs.* Adhesions may materially influence symptoms; these may prove the cause of acute or chronic conditions in accordance with the organs included and the resulting distortion or occlusion. The organs included are the liver, stomach, duodenum, transverse colon, omentum, pancreas, and right kidney. The gall-stones with such complications may be entirely overlooked in the presence of the grave secondary lesions.

Pyloric obstruction, without the history of previous acute attacks or chronic symptoms sufficient to create the suspicion of gall-stones as the primary and causative condition, may develop and threaten life. Such cases and other mechanical defects due to adhesions which cause symptoms can only be saved by surgical interference.

Cholelithiasis without colic may lead to secondary changes near or distant which demand attention that life may be saved. The accompanying *infection of the bile passages and gall-bladder may be either acute or chronic;* in some cases subjective symptoms may yield during limited periods. Exacerbations are reasonably certain and unless there is free drainage one of many dangers must be faced. The recognition of the true condition is often difficult, and many are found septic with the heart and kidney deeply involved or there may be, as was recently found in the case of a colleague, advanced amyloid disease with disseminated liver infection. Such conditions are fatal; they can be prevented; and life may be saved by reasonably early vigorous and radical treatment. The further results of chronic cholelithiasis are considered in this section under the head of "Complications and Remote Results." It is safe to conclude that in latent cases which are made active by added infection, symptoms will persist—are either continuous or intermittent—and the resistance of the patient will be taxed in accordance with the virulence and extent of the secondary changes, whether acute or chronic. The prognosis will, under such conditions, depend entirely upon the ability to remove the focus of infection and drain the bile passages. In the chronic cases

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with acute or chronic infection, the dangers of feeble resistance, hemorrhage, shock, nephritis, myocardial insufficiency, cholemia, and a variety of other complications materially influence the outcome.

(c) Obstruction of the Common Duct

Courvoisier considers gall-stones in the common duct dependent upon one of three possibilities: their passage to the duct from the gall-bladder, their entrance through the hepatic ducts, or their formation *in situ.*

The majority of stones in the common duct cause only partial obstruction. The symptoms and changes produced are dependent upon the size and the situation of the stone in the duct. *Untreated stone in the common duct finally produces changes not only in the duct, but also in the gall-bladder, the smaller bile passages, and in the liver tissue.* In the duct, when the passage of bile is prevented there is dilatation, and infection is invited. *Cholangitis is usual.* With small gall-stones plugging the passage, bile may find its way into the duodenum; with a single large stone and secondary changes it is not uncommon to find the obstruction partial and bile entering the intestine. *If the obstruction is complete, the jaundice is deep and unyielding.* In these cases the surprising feature is *the effect of the occlusion on the gall-bladder* which is evident in most but not in all cases. This has been formulated and is known as the *Courvoisier's law:*

With obstruction of the common duct by gall-stones the gall-bladder does not enlarge. It is atrophied and if it holds gall-stones it is contracted upon them, while with cancer and obstruction, either within or without the duct, (usually there is invasion of the pancreas) the gall-bladder is enlarged and palpable, and *atrophy results in only one-twelfth of the latter obstructions (Courvoisier's Law). Dilatation of the bile ducts behind the stone* is the rule; the *hepatic* and *intrahepatic ducts* are often so dilated as to admit the index finger (Bland-Sutton).

Long continued pressure of an incarcerated stone in the common duct or associated infection often causes ulceration with the discharge of the stone into the duodenum. Such outcome is favorable and in most uncomplicated cases is followed by recovery and the passage of the stone.

Nature seeks to establish "adventitious outlets" for the bile with complete obstruction of the common duct, and thus saves life. The resulting *fistulae* afford drainage into the intestine and make the prognosis of uncomplicated jaundice due to gall-stones favorable (Naunyn, Bland-Sutton). Among the more serious complications are *liver abscess, suppurative cholangitis, thrombosis of the portal or other large veins, aneurism of the hepatic artery, septic pneumonia, empyema, and acute or chronic pancreatitis.* In a number of cases chronic sepsis ends life unless the cause is removed.

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From the preceding statements it is apparent that gall-stones in the common duct may induce local changes and distant serious disturbances. *Liver abscess* due to occlusion by stone of the common duct is more likely to occur than with any other obstruction, and *ulcerative perforation* is comparatively frequent. With the *ball valve action* of a stone in the common duct the symptoms are intermittent including the hepatic fever of Charcot, jaundice, and recurring biliary colic. The prognosis of such cases is not bad; the symptoms may recur during many years without materially lowering the resistance of the patient, but unless nature overcomes the recurring obstruction or it is relieved by radical means, the prognosis for cure is unfavorable and local or distant complications may end life. The absence of added infection in these chronic cases for many years is often striking and favorable.

(d) Obstruction of the Cystic Duct

Gall-stones held in the cystic duct originate in the gall-bladder; they may increase in size by aggregation. In 255 post mortems of gall-stone disease in Basel, 17—6.7 per cent—were in the cystic duct, and in Erlangen there were 16 of 343—4.6 per cent (Courvoisier)

Lawson Tait taught that the acute symptoms due to stone in the cystic duct were more violent than when in the common duct. This is so, Tait held, because of the difference in the caliber of the two tubes in most cases. Courvoisier and others deny the anatomic cause given by Tait and contend that Oehme's measurements do not justify the former's conclusions.

When the stone is held in the duct, *dilatation of the gall-bladder* usually results. Gradual obstruction of the cystic duct by gall-stones may cause but few or no symptoms during considerable periods, and without dilatation or colic and atrophy of the gall-bladder may escape detection. Courvoisier reports 30 of 97 cases in which the stone was held in the cystic duct in which *atrophy of the gall-bladder resulted.* The frequency of atrophy of the gall-bladder (in 1/3 of all cases of stone in the cystic duct) has been overlooked by clinicians.

The *dilatation of the gall-bladder* due to stone in the cystic duct is known as *"dropsy of the gall-bladder," "hydrops vesicae felleae" and "ectasia".* It offers an excellent prognosis when the diagnosis is followed by free drainage and the removal of the offender. *Dilated gall-bladder resulting from cystic obstruction* may reach enormous size and may simulate cystic kidney, hydro- and pyo-nephrosis, and ovarian cyst. *"Riedel's lobe,"* a tongue-shaped bit of liver connected with the right lobe, may project from the anterior margin and present over the enlarged gall-bladder. *Obstruction of the cystic duct may be borne during long periods even*

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with dilated gall-bladder. The dangers are due to infection, perforation, peritonitis, liver abscess, cholangitis, and acute or subacute pancreatitis.

Small gall-stones in the cystic duct may cause enormous enlargement of the gall-bladder, and often larger stones may be associated with less dilatation. With these—one or more—the duct may dilate, adhesions result, and because of ulceration, fistulous openings may follow into the stomach (cystogastric fistula), into the duodenum (cystoduodenal fistula) or into the transverse colon (cystocolic fistula).

(e) Obstruction of the Hepatic Duct and Intrahepatic Ducts

Gall-stones in one of the hepatic ducts, in the smaller ducts or in the liver substance, are almost always coincident with gall-stones in other passages—usually in the common duct. In 56 of 59 collected cases of gall-stones in the hepatic ducts there were stones in other parts of the liver, and in 51 cases of gall-stones in the hepatic duct there were 45 in which the common duct was obstructed and displaced, or there had been previous operations (Courvoisier). These statistics show further that in 24 of 45 cases of hepatic duct calculi there was stone in the common duct, or dilatation due to previously incarcerated calculi; in 6 cases there was narrow constriction, and in 2 compression of the duct due to hydatid in one, and cancer of the pancreas in the other.

Unquestionably the impeded flow of bile, usually because of occlusion of the common duct, is the powerful factor in the causation of cholelithiasis, within the hepatic tree (Courvoisier).

The *prophylaxis* of hepatic calculi must depend almost entirely upon the radical and early removal of gall-stones within the common duct and the prompt relief of all organic constriction. *Rupture of the hepatic duct* due to stone is not frequent, but there are recorded cases in which death was prompt and in most of these there was septic peritonitis with pus and blood in the abdominal cavity.

Multiple or single stones are found at times in the liver substance (intrahepatic ducts), usually of the bilirubin-calcium variety (Bland-Sutton). This condition when multiple and disseminated, offers but little hope of relief by surgical means. In many cases these gall-stones cause no symptoms and are recognized post mortem. In framing the prognosis of all gall-bladder disease it must be conceded that the long continued presence of gall-stones in the gall-bladder and the continuous excretion of irritating and poisonous products through the bile current provoke precipitation and gall-stone formation in the intrahepatic bile passages (William Hunter).

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(f) Complications and Remote Results

The presence of gall-stones in the bile passages is always a menace. Ten per cent of all autopsied bodies have gall-stones, and of this number 95 per cent never had symptoms which suggested their presence. In those cases which cause symptoms, the complications and remote results are so numerous and far-reaching as to make their full consideration impossible within the space available in this volume. Reference has been made to the many results of associated infection and their dangers, the frequency of gall-stones with or following the graver infections—typhoid fever, pneumonia, etc.

In the prognosis the insidious changes which are produced in the immediate surroundings of the stone are of importance, as already shown in the preceding pages. These changes always depend upon a number of factors, the most important of which is infection. The number of stones held in the gall-bladder is not the important factor, for in the presence of hundreds of faceted gall-stones, closely packed within the thickened wall, there may be no subjective symptoms and no complications; on the other hand, with an equal number or but few stones and added infection, or as the result of pressure, adhesions, or from a variety of causes, life may be threatened by one or more of almost countless complications. The leading complications besides those already mentioned are referable to the *peritoneum, intestines, stomach, liver, pancreas, kidney,* and *cardio-vascular system;* while the *vagaries and wanderings of gall-stones* in individual cases may lead to the invasion of other organs, unsuspected, because of their distance from the original seat of the stone.

One fact of enormous prognostic value stands out prominently and that is that the protective powers—the factors of safety—are almost always stimulated by the presence of gall-stones by which subsequent complications are anticipated, and their dangers are reduced, so far as it is possible. Such conservative effort is prominent with *perforation by gall-stones,* with *ulceration,* with *fistulous openings* through long or short avenues. *In cases of perforation or ulceration without protective adhesions, general* or *local peritonitis may often prove promptly fatal.*

Perforation of the gall-bladder is not frequent in spite of its enormous dilatation. The *distended and inflamed gall-bladder may cause peritonitis without perforating.* With such complication the acute manifestations of peritonitis may be absent; the course may be subacute; ascites finally develops.

The *gangrenous gall-bladder, without perforation,* may at first cause localized peritonitis which may become diffuse unless radical surgical treatment is promptly instituted.

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Fistulae.—Perforation into the duodenum is a frequent result of chronic cholelithiasis and if the stone is not too large, it passes without further incident; the local changes may never again cause symptoms.

Adhesions of the gall-bladder and duodenum or pylorus may form a mass with symptoms of obstruction and stagnation simulating cancer of the stomach during indefinite periods. In one of my cases after repeated gall-stone colic there was a tumor simulating cancer of the stomach with symptoms of pyloric obstruction during 15 months; the disappearance of the tumor was promptly followed by intestinal obstruction, the passage per rectum of an enormous gall-stone weighing 15 grams (240 grains) 5 cm. (2 inches) long and 7.5 cm. (3 inches) in circumference (Elsner). The simulation of pyloric cancer by gall-stones is not without parallel; in most reported cases the prognosis proved to be good. Life was saved either by surgical interference or by ulceration, as in our case, and the passage of the stone (Pepper, Miles, Fiedler, Ross, Hale White, Ogle and Courvoisier).

The wanderings of gall-stones, their vagaries, and the protection offered by adhesions are often surprising. The distance to which stones may travel is often remarkable. I have accumulated a large number of histories with post mortem examinations which prove the remarkable tolerance of the aberrant gall-stones in new locations (Elsner).

The route from the gall-bladder into the duodenum by protective adhesions first, and then ulceration, is almost as frequent as the *external* or *cutaneous fistula*.

Naunyn's material offers the following figures:

Cutaneous fistulae, usually opening near the umbilicus	184
Gastrointestinal fistulae	108
Fistulae between the common duct and duodenum	15

Courvoisier found perforation directly into the peritoneum in 70 of 119 cases, and in 49 the free peritoneum was protected by an encapsulated abscess.

My material included the case above mentioned of enormous stone which for 15 months caused symptoms of pyloric obstruction and final intestinal obstruction after it traveled down the intestine. In this case the symptoms of intestinal obstruction were complete, operation was decided upon, and while the preparations were being made the stone passed spontaneously per rectum. The patient made a full recovery after passing a second larger stone several weeks after the first.

Infectious cholecystitis, cholangitis, empyema of the gall-bladder due to gall-stones in another case, were associated with complete obliteration of the cystic and common ducts with probable primary duodenal ulcer in which there was burrowing of the stone into a bed of fibrous tissue pro-

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vided by nature. This patient made a full recovery after cholecystotomy and final choledochoduodenostomy.

Another experience less favorable was the wandering of a larger gall-stone through a fistulous opening with numerous dilatations into the retroperitoneal space lodging finally in pancreatic tissue. Pancreatic cancer was simulated during several months. The post mortem cleared the horizon.

Migration of gall-stones with or without abscess formation into the right kidney, with repeated attacks of renal colic, in one of my cases ended in the death of the patient. Courvoisier collected seven cases of *urinary fistulae* associated with gall-stones; six of these were in women. Pelleton and Barraud report two hundred gall-stones passed by a woman per urethram in eight days. The last stone was caught in the urethra, but was easily pushed on from the vagina. The patient recovered.

The histories of similar cases are included in Langenbuch's material, and prove the tolerance and protective methods of nature and the relatively good prognosis. Patients with *biliary* (*cutaneous*) *fistulae* may live during many years and finally die of intercurrent disease or infection. In some of these cases the fistula may close during varying periods, finally open to allow the escape of one or more stones, or remain permanently closed. The long continued presence of gall-stones may lead to such enormous *dilatation, distortion,* and *adhesions with aberrance of gall-stones* as to preclude the possibility of operation. Such patients may live during long periods barring accident due to the gall-stone disease, but with added infection the prognosis is bad.

Bronchobiliary Fistulae.—Gall-stones may cause fistulous opening into a bronchus through an abscess following infectious cholangitis, adhesions of the diaphragm and the lung and rupture into the latter, or as Rolleston suggests the perforation may be into the pleura primarily, and then into the lung. *Subphrenic abscess* may result from perforation of the gall-bladder and from this opening into the diaphragm, and finally into the lung results. Mandard reports the perforation of the gall-bladder directly through the diaphragm into the lung. Recovery from bronchobiliary fistula is often spontaneous; once healed the tract is not likely to reopen, but relapse may occur. The removal of the primary focus where possible is likely to lead to cure.

Ulceration into the portal vein and into the hepatic artery are rare accidents, but it does occasionally happen and with fatal results. Kehr's case mentioned in connection with aneurism of the hepatic artery was an exception.

Chronic cholelithiasis with added chronic infection, continuous or intermittent, is unquestionably instrumental in inviting arterial and renal degeneration.

The *frequency of arteriosclerosis and interstitial nephritis with gall-*

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stones is striking and not accidental. Mosher found that of 115 cases of cholelithiasis, 50 or 43 per cent had arteriosclerosis. Moore has shown that interstitial nephritis increases the liability to cholelithiasis in women.

Moore's statistics are exceedingly valuable and we quote them:

"In 261 cases of granular kidney with an average age of 56 years, there were gall-stones in 56, or 21.4 per cent (average age, 59 years). In 49 cases of large white kidney, with an average age of 40, there were gall-stones in 2, or 4 per cent; and in 47 cases of small white kidney, with an average age of 34 years, gall-stones were present in 1, or 2 per cent. The greater incidence among the cases of granular kidney does not, as might at first sight appear, depend on the greater average age alone; for among the 261 cases of granular kidney there were 36 between the ages of 32 and 42 (thus including with a margin the average ages of the large white and small white kidneys), in 6 of which, or 16.7 per cent, there were gall-stones. Of these 36 cases, 11 were women, 4 of whom had gall-stones—or 36 per cent—and 25 men, 2 of whom—8 per cent—had gall-stones. Of the remaining 225 cases of granular kidney there were 138 men, 21 of whom—15.2 per cent—had calculi, and 87 women, 29 of whom—33.3 per cent—had calculi. The increased incidence of gall-stones in granular kidney therefore appears to be due to the high incidence of cholelithiasis in women with granular kidney. In the 261 cases of granular kidney the women were to the men as 3 to 5. The incidence of gall-stones in the 98 women was 33 per cent, and in 100 consecutive women over 40, dying in St. George's Hospital from all kinds of diseases, the incidence of gall-stones was 25 per cent."

In all of these cases the prognosis is darkened by the associated and progressive *myocarditis.* Endocarditis is a frequent association. The association of *pancreatic disease with cholelithiasis* is fully considered with the prognosis of pancreatitis (See Pancreatic Diseases).

The long continued irritation due to gall-stones unquestionably leads to *cancerous degeneration* of the organ harboring it, but it cannot be assumed that malignant disease in distant organs is stimulated by the presence of gall-stones. Cancer will be found associated with gall-stones in 2.25 per cent of operated cases.

Intestinal Obstruction.—Obstruction by gall-stones may be either complete or partial. In most cases with a stone of sufficient size to cause intestinal obstruction there is a palpable tumor which disappears from its original habitat and wanders on until it is caught in the intestine, causing during varying periods depending upon the degree of obstruction and the acuteness of its onset, a train of characteristic symptoms with visible peristaltic unrest, particularly if the obstruction is partial. Sudden acute complete occlusion is at once life-threatening, and can only be relieved as a rule by prompt surgical treatment. There are exceptions to this statement, but in the light of the experiences of the present day,

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including the results of surgical operation, it is unfair to the patient to reach a conclusion which would justify procrastination in these cases.

When large stones pass from the gall-bladder into the intestines, ileus or obstruction is to be expected in almost 40 per cent of such cases. Courvoisier reports ileus in 28 of 73 cases—38.3 per cent. The majority of stones are dislodged and pass per rectum. The prognosis is more serious when ileus follows gall-bladder duodenal fistulae than when the opening is into the colon. Of 30 fatal cases 22 were due to gall-bladder duodenal fistula, and only 2 to gall-bladder colon perforation (Naunyn). If a gall-stone finds its way into the duodenum through the common duct there is but little danger of intestinal obstruction. Symptoms of intestinal obstruction with changing position of the mass prove that the stone is being pushed by peristalsis; in such cases the prognosis is good. Robson says: "If it were possible to be certain that a gall-stone was the cause of the block, the expectant form of treatment would be fully justified, since the probability, arguing from published cases, is that the gall-stone would eventually pass."

Cases in which there are "diagnostic difficulties" throw an enormous responsibility on the surgeon if he waits for nature's cure. It is true that 50 per cent at least of the cases recover without operation, that the obstruction may not yield for several days; Gray reports one case in which the stone was dislodged after 12 days, with full recovery. The encouragement which such experiences strengthen leaves the remaining 50 per cent seriously handicapped and the majority of these are therefore operated after necrosis of the intestinal wall, and circumscribed or diffuse peritonitis are fully developed. Langenbuch takes the extreme view which seems justified in these days of splendid technic and early operation and makes the unqualified statement that "gall-stone obstruction is a surgical disease, the treatment of which is to be entrusted to the physician only during a very short period," if the prognosis is to be favorable.

A diverticulum containing a stone may be associated with mechanical obstruction of the intestine. Gangrene may follow. Gall-stones may find their way into Meckel's diverticulum and into the appendix. In both infection is invited, and unless relieved serious results are likely to follow.

Hemorrhage.—In many cases of prolonged obstruction of the common duct with jaundice, the blood condition invites hemorrhage and often makes operation hazardous. The prognosis of gall-stone operations on such patients as show the hemorrhagic tendency is often favorably influenced by preparatory treatment, including the injection (secundum artem) of blood serum—preferably rabbit serum—after the question of possible anaphylaxis has been thoroughly considered.

Symptoms referable to the nervous system usually yield with the removal of the stone, but persistent jaundice due to long continued gall-stone impaction may cause alarming brain symptoms and occasionally

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insanity. One of my patients, an old man, became violently insane, but was relieved after a cholecystotomy. In another case prolonged cholemia due to obstruction of the common duct caused confusional insanity.

Surgery and Cholelithiasis

In considering the prognosis of gall-stone disease our conclusions must be materially influenced by the brilliant results of surgery in the radical treatment of diseases of the gall-bladder and biliary passages. Early operations in uncomplicated cases "is an innocent and simple operative procedure" (Jacobson). W. J. Mayo giving his experiences in 4,000 operations on the gall-bladder and biliary passages which he and his brother have performed, found the average mortality 2.75 per cent; 11 per cent of the total number of deaths occurred in patients with cancer. The Mayo experience proves that "simple operation for uncomplicated gall-stones has had a mortality of less than 0.5 per cent, and this might be called accidental, since it was due to the condition of the patient rather than to the operation."

"Fatalities can be traced in almost every instance to delay." My conclusions justify the accentuation of the fact in spite of the escape of the majority who harbor gall-stones that in the bile passages they are always a menace, not only to the organ which harbors them, but they may suddenly or gradually lead to pathological processes, benign or malignant, near or distant, giving rise to unexpected and serious conditions. As I have elsewhere in this section remarked, a large number of patients with indefinite symptoms are suffering from chronic infection with gall-stones. In almost all radical treament is followed by a return to health.

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L. Diseases of the Pancreas

1. Pancreatitis

Pancreatitis may be either (a) *acute* or (b) *chronic.*

(a) *Acute Pancreatitis*

Acute pancreatitis is almost always hemorrhagic, and the varieties which are characterized as *gangrenous* and *suppurative pancreatitis* are not independent conditions—*ab initio*—but represent the advanced stage of hemorrhagic pancreatitis. Gall-stone disease is the leading provoking factor; traumatism and alcoholic excess with local lesions are also etiologic factors. Most cases are in men above the ages of fifty years.

Deaver says: "The common bile duct is the crucial point of the whole biliary system, as it is the outlet for the biliary secretion and by its anatomic relations wields an important influence over the pancreatic function. The pancreatic portion (of the common bile duct) lies in a groove in the posterior surface of the head of the pancreas and extends from the inferior border of the first portion of the duodenum to a point where

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the duct enters the wall of the descending or second portion of the duodenum. In two-thirds of the subjects this portion of the bile duct is completely surrounded by pancreatic tissue." "The opening of the common duct is usually above that of the duct of Wirsung." The two are separated by a thin layer of mucous membrane. The duct of Santorini is "always present and anastomosis with the duct of Wirsung within the pancreas is about 90 per cent of cases." In 50 per cent of all cases the duct of Santorini is obliterated or constricted; hence when the duct of Wirsung is closed, it cannot under such conditions assume its functions. Usually the common bile duct and the duct of Wirsung open at the ampulla of Vater. "The apex is situated at the summit of the diverticulum and is their common duodenal orifice." It is easy therefore under anomalous conditions of the mucosa for the bile and intestinal content to find its way to the pancreas. Occlusion of the ampulla (papilla) of Vater by a gall-stone, a plug of mucus, or because of catarrhal swelling or cicatricial change following ulcer, may turn the bile into the pancreatic duct and lead to pancreatitis. Unless the duct of Santorini is patent there is no means of escape; Opie found this to obtain in less than 50 per cent of his cases.

Traumatism may cause the sudden development of *acute hemorrhagic pancreatitis.* In these cases the evidence of shock and collapse with symptoms which simulate acute peritonitis, with great abdominal pain—at times symptoms of intestinal obstruction—without fecal vomiting, and but little or no fever and rapid pulse, at once prove the gravity of the condition. When there is a large loss of blood the patient may not rally. The average duration of life is between 2 and 3 days. I had one case in which there was arteriosclerosis with advanced disease of the abdominal aorta and rupture of the pancreatic vessel; the hemorrhage was large, the symptoms simulated intestinal obstruction during the first 24 hours; the patient lived between 12 and 13 days. The diagnosis of hemorrhagic pancreatitis was corroborated post mortem. In cases of gastroduodenal catarrh usually recurrent, which may or may not be associated with gall-stones or cholangitis, pancreatitis may develop. These cases at times show gangrene of circumscribed portions of the gland. The bleeding is not always limited to the pancreas but the surrounding tissues may be infiltrated, particularly the fat tissue including the mesentery, mesocolon and omentum, also the regions of the left kidney (Fitz and Wood).

With *hemorrhagic gangrenous pancreatitis* there may be localized peritonitis; diffuse peritonitis is the exception. *Disseminated fat necrosis* is a frequent complication of pancreatitis. *Fat necrosis* which is considered pathognomonic of acute pancreatitis depends upon the ferment action upon the gland and its secretion (trypsin) when there is obstruction to its outflow. The fat necroses may be widely spread throughout the omentum, mesentery and the fat tissue of the body.

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Suppurative pancreatitis may follow the hemorrhagic, complicate it, and involve the adjoining tissues, thus converting the lesser omentum into an abscess cavity. This may rupture in one of several directions, usually into the stomach or duodenum, or form a subphrenic abscess.

Secondary infection may involve the veins, causing *purulent thrombosis* or *abscess of the liver;* the *pleura* and *pericardium* are occasionally involved; *perforative peritonitis* is rare.

Hemorrhagic gangrenous pancreatitis is always a grave disease, and usually causes death from shock within 24 to 60 hours. If patients with hemorrhagic pancreatitis live and develop gangrene they become profoundly septic, and die within 4 to 8 weeks.

Suppurative pancreatitis may become chronic, the patients living several months or longer with evidences of sepsis and diabetes. Fitz feels that his experience justifies the statement that "the prognosis is not absolutely hopeless however, since evidences of antecedent pancreatitis have been found repeatedly at post mortem examination." The self-digestion of the gland (by trypsin) is an important factor. The value of the *Cammidge test* is questionable for diagnosis and prognosis. Cammidge holds that the reaction is positive in acute pancreatitis and that it makes the differentiation of intestinal obstruction possible and that chronic pancreatitis can be differentiated from gall-stones. Osler says "the reaction is negative in about three-fourths of malignant disease." Reports from the Mayo clinic offered by Wilson led him to the conclusion that without the clinical histories and other factors "the end results judged by Cammidge's own criterion must be considered as a means of diagnosing disease of the pancreas, as both valueless and misleading." I do not recommend its consideration for prognostic purposes. (The method of carrying out the test is fully given by Latham and Torrens. See References at end of chapter.)

The prognosis of the acute cases depends largely upon the ability of the surgeon to remove or overcome the primary cause. Where this can be accomplished the early operation offers considerable hope. Much will depend on the discriminating sense of the surgeon in deciding upon the opportune time for operation. Concerted action of the physician and surgeon will always be necessary from the moment of diagnosis or suspicion of pancreatitis.

Deaver has called attention to the importance of *pancreatic* and *peripancreatic lymphangitis*, and believes that certain cases of acute hemorrhagic pancreatitis are due to infection of lymphatic origin.

(*b*) *Chronic Pancreatitis*

There are a variety of causes of chronic pancreatitis. Among these are chronic or recurrent gastro-intestinal catarrh, gall-stones, chronic

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alcoholism, obstruction to the pancreatic duct from pressure without, or organic change within, calculi, neoplasms, cicatricial change and adhesions due to ulcers of the stomach or duodenum; Fitz mentions caries of the spine and aneurism, and in infants congenital syphilis. Typhoid, colon and streptococcus infection have also been responsible.

Sclerosis of the head of the pancreas resembling cancer is not uncommon. The disease may be either *interlobular* or *interacinar*. In the former, the sclerotic change rarely includes the islands of Langerhans, in the latter (interacinar) there is productive change between the acini without much inclusion of the interlobular tissue. *Arteriosclerosis* may also cause interstitial chronic changes in the pancreas.

Diabetes mellitus is often due to *fibrosis of the pancreas* (See Diabetes Mellitus and the Pancreas). Chronic pancreatitis often causes indefinite symptoms of ill health with faulty digestion and anorexia, fat stools (not pathognomonic), some jaundice, abdominal pain during long periods. In another class of cases there are persistent symptoms of *chronic gastritis*. If the disease advances, diabetes is fairly certain to develop; it may develop early. There are cases which remain stationary. The productive changes cannot be overcome; if the atrophy is advanced and the islands of Langerhans are included, life as a rule is threatened. Fitz holds that permanent glycosuria and chronic pancreatitis is a fatal combination (See Diabetes Mellitus).

2. Hemorrhage

(*Pancreatic Apoplexy*)

It is exceedingly difficult to differentiate hemorrhage and hemorrhagic pancreatitis. There are cases in which, without warning, there is a sudden and depleting hemorrhage into the pancreas with prompt death. With the *purpuras* we occasionally meet such an accident, also with arteriosclerosis, the acute infections, with chronic alcoholism, and cirrhosis of the liver. Fatal hemorrhage may occur during the early hours of acute pancreatitis; it may develop suddenly with gangrene during the terminal stage of hemorrhagic pancreatitis. The prognosis of hemorrhage depends upon the extent of the bleeding, the damage to the gland, the resistance of the patient, and the cause. There are probably many small hemorrhages into the pancreas which cause no symptoms, but generally the prognosis of pancreatic hemorrhage may be considered grave and the majority die before the end of 48 hours. In one of my cases the patient died within 3 hours. His initial symptom was severe epigastric pain, sudden collapse; there was no radial pulse palpable for over 2 hours before death. Those who live beyond the period of collapse face the dangers of acute pancreatitis.

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3. Necrosis of the Pancreas

We have referred to *fat necrosis* in connection with acute pancreatitis. Fat necrosis may accompany any of the diseases of the pancreas because of self-digestion. Fat necrosis is comparatively frequent after traumatism. The condition is said by Minkowski to be more frequent in advanced life. Its leading clinical features are sudden and progressive symptoms which are suggestive of perforative peritonitis which lead to death in from 24 to 72 hours.

When fat necrosis is limited, patients may live during several weeks, but this is the exception. *Large necrotic foci or destruction of the entire pancreatic tissue are uniformly fatal.* Necrosis may precede suppuration (abscess). In the mild and circumscribed cases, the tolerance for sugar is found reduced—a symptom of diagnostic and prognostic value.

Pancreatic necrosis is never to be lightly regarded. Recovery from the initial collapse should not delude the attendant to believe that an absolutely favorable prognosis is justified, for following this there may be fever, deep toxemia, and finally cardiac asthenia. Surgery offers the only hope in most cases.

4. Pancreatic Calculi

We rarely see pancreatic calculi. Medical literature gives comparatively few histories of the disease. The chemical constituents are carbonate and phosphate of lime. The origin of these stones (they are usually multiple) is due to stasis and infection. A number of the cases will be accidentally discovered post mortem. Some have escaped during severe colic. When they remain *in situ* they may cause secondary changes characteristic of chronic fibrotic pancreatitis, cysts, and abscesses; some hold that their continued irritation may cause carcinoma (?). With symptoms justifying the suspicion of their presence and continuous ill health, surgery offers hope of successful removal.

5. Pancreatic Cysts

The clinical experiences of Körte who reported 121 cases operated, 60 males and 56 females, showed over half beyond 40 years of age. Pancreatic cysts have been found in early life—no age is exempt.

Cysts which arise suddenly after traumatism, promptly recognized and operated early, offer, in the absence of complications, an excellent prognosis. Cystic tumors developing in the midst or as a sequel of infection, or with evidences of active inflammatory change, are less favorable, but many of these yield to radical treatment. There are cases with the history of surprising chronicity in which the cause is unknown which

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live during many years. Körte classifies pancreatic cysts as (a) retention (due to occlusion of the main duct), (b) proliferation (cystoadenoma), (c) retention cysts (alveolar and smaller duct obstruction), and (d) false cysts.

The anatomic location of the cyst between the stomach and transverse colon may be demonstrated by means of the Röntgen rays in most cases, and by physical examination. It is possible when there is not complete occlusion that the cyst may empty itself from time to time. The dangers are pressure symptoms, hemorrhagic or chronic pancreatitis, with fat necrosis, exhaustion, and final permanent glycosuria. Surgery saves over 90 per cent of cysts. The possibility of self-cure in the presence of a positive diagnosis ought not to exclude radical treatment.

6. Pancreatic Neoplasms

Cancer of the head of the pancreas is the most frequent neoplasm, and develops after the age of 40. In these cases jaundice, loss of flesh, palpable tumor, at times inordinate appetite and ascites, are the leading features. Diabetes has complicated some. In 6,300 cases of internal disease I have had three pancreatic cancers. At the Allgemeine Krankenhaus in Vienna among 18,069 post mortems, 22 cases of cancer of the pancreas were found. Hale White found 20 cases in 6,000 autopsies. Osler reports in 1,500 autopsies at the Johns Hopkins Hospital 6 adeno-carcinoma, and one doubtful case, with 8 cases of secondary malignant deposits in the pancreas.

Prominent among the symptoms was persistent salivation with a dry glazed tongue and, as above suggested, an inordinate appetite. Food, however much is taken, does not prevent the progressive loss of flesh and increasing enfeeblement. Jaundice remains, "does not disappear at any time"; deep jaundice and petechiae are terminal symptoms.

I have never in my practice seen a *sarcoma of the pancreas.*

Tuberculosis of the pancreas is considered among the infections (See Section I).

Syphilis of the pancreas is also considered with visceral syphilis (Section I).

Prognosis of cancer is clouded by the fact that in almost all cases the diagnosis is not made until the disease has advanced. Early recognition and prompt operation offers the only hope.

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Section VI

Diseases of the Kidney

Anomalies of the Urinary Secretion

THE PROGNOSTIC SIGNIFICANCE OF:

(a) *Albuminuria*

General Considerations.—Scarcely a chapter in this work fails to impress the reader with the fact that albuminuria is frequent and symptomatic; to understand its clinical significance fully demands close investigation of *all* that the individual case offers. Its prognostic significance cannot be determined without a full consideration of the associated urinary changes; indeed, the microscopic picture is always more important than is the chemical, and with many acute and chronic diseases in the presence of albuminuria, the functionating ability of the kidneys and heart, the ability to prevent renal insufficiency and other complications are among the leading and most important factors.

Albuminuria is the presence of serum albumin in the urine. With serum albumin there is always an admixture of *serum globulin;* the latter is of but little prognostic significance in most cases. No attempt has yet been successful to take advantage of the varying ratio of serum albumin to globulin as an aid in the prognosis of disease. The quotient is so variable according to Paton—from 0.6 to 39—"as to deprive it of much prognostic value" (Dixon Mann).

There are surprising variations in cases of benign nephritis without clinical evidences of increase of symptoms, without evidences in the clinical history of increasing change in the glomerular apparatus; while occasionally it has been found that during the terminal stage of nephritis there is a striking and continuous increase of globulin in the urine. Mann believes that this is due to "denudation of some of the tubular walls. Under these conditions the excess of globulin usually indicates that the end is near." With *amyloid kidney* there is often a preponderance of globulin over serum albumin (Senator, Joachim); there are cases

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in which the opposite is true (Noel Paton, Petri). In all of these the process is secondary and fatal.

Nicholas Cotugno toward the end of the eighteenth century (1770) called attention to the coagulation of the urine in certain forms of dropsy. Early in the nineteenth century Richard Bright, one of the three geniuses of Guy's Hospital (the others were Addison and Hodgkins, 1827) clearly demonstrated to the profession, the clinical and prognostic significance of albumin loss with the urine in certain conditions, associated more particularly with the dropsies. Normal urine contains an unrecognizable infinitesimal trace of albumin.

For diagnostic purposes it is sufficient to recognize *two varieties of albuminuria:*

(1) False Albuminuria.
(2) True Albuminuria.

When albumin is demonstrated by the usual tests it should be considered abnormal.

(1) False Albuminuria.—*With false albuminuria* the albumin finds entrance to the urine outside the tubular apparatus of the kidney; it is therefore proper to consider it to be of *extra-renal origin. The leading sources of extra-renal or false albuminuria* are from the genito-urinary tract, including the kidney pelvis to the meatus urinarius. The majority of such albuminurias are surgical, due to stone (pyelitis calculosa), bladder and ureteral lesions, including cystitis, gonorrhea and leukorrhea, menstrual discharge, etc.

(2) True Albuminuria.—True albuminuria may be either (a) hematogenous, (b) parenchymatous or (c) vascular.

(a) **Hematogenous albuminuria** is due to alterations in the diffusibility of the blood, more particularly the blood albuminoids, owing to changes in the salts of the blood or the alkalinity of the serum; it is never due to the excretion of undigested or partly digested albumin from the food.

(b) **Parenchymatous albuminuria** is due to changes in the glomerular and tubular apparatus of the kidney.

(c) **Vascular albuminuria** is due to changes in the walls of the renal vessels (glomerular apparatus) which may be affected by toxic agents, inflammatory conditions, vasomotor changes, or altered blood pressure.

Physiological Albuminuria

The statement is above made that *albumin is always present in normal urine, but I must again accent the fact that when its presence is made clear by the ordinary tests used in the laboratory of the clinician it should be considered abnormal if it is persistent or recurs on slight cause. For prognosis it should be remembered that the diagnosis of physiological*

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albuminuria is not justified except with moderate albuminuria without symptoms of disease, without dropsy, without heart changes and without arterial lesions (*Leube's rule*).

Albuminuria in normal newborn infants is of common occurrence. Heller found it at least once in each of 31 normal infants. Franz and von Reuss have graphically demonstrated the frequency of albumin during the first few days of life.

The acute clinical observer may at long intervals feel justified in diagnosticating "physiological albuminuria" and prognosticate accordingly, but experience will prove exceptional in which close observation with recurring albuminuria finally justifies the diagnosis, for in the end the majority of such diagnoses are changed to chronic nephritis. Even the occasional presence of albumin in the urine, in suspected cases, which has been voided before the patient arises, never justifies the diagnosis of physiological albuminuria; such cases are, when of renal origin, an expression of true nephritis. Granger Stewart wrote: "Led by the contradictory results I experimented anew and concluded if albumin is present in healthy people it was barely discernible after delicate tests, even after concentration of the urine; if present it is accounted for by transudation with the urine, or from epithelia or other cellular elements from the genito-urinary tract."

It cannot be denied that *active exercise in otherwise healthy individuals may cause transitory albuminuria, but even such cases should be carefully studied before a prognosis is justified which has its basis on the diagnosis of physiological albuminuria.* Leube, it is true, found of 119 soldiers 4 per cent with albuminuria on arising in the morning, and 16 per cent of these showed albuminuria after a morning march. These figures—4 per cent of albuminurias—correspond very closely with the results of the urine analysis of life insurance applicants which we have made and in which as a rule true albuminuria was finally found to be of renal (nephritic) origin.

For diagnostic as well as prognostic purposes, "physiologic albuminuria" may well be considered a misnomer. Crofton agrees and says: "I consider this term a misnomer, for a biologic phenomenon because it is innocent need not therefore be physiological. It is better always to regard the excretion of serum albumin as a pathological phenomenon." In the end, in the prognosis of these unexplained and supposedly innocent albuminurias in which positive evidences of kidney lesion are absent, some toxic or nutritional fault should be suspected if the urine repeatedly shows the presence of albumin.

Albuminuria following exercise, cold bathing, emotion, chilling of the surface, epileptic seizures, or indigestion will rarely prove to be "physiologic" but will be found to depend upon transitory circulatory disturbances or metabolic faults which are usually toxic. For the purposes of

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prognosis in these cases the results of experience prove the reliability of Osler's conclusion that "the cause must be something unusual and excessive—as a very hard tramp, a football match, a race, etc." *When albuminuria without other evidences of renal change recurs at long or short intervals even without casts, for which no extra-renal cause exists, it is always suggestive of change in the kidney and in the majority of such cases associated conditions finally make the diagnosis positive.*

Renal albuminuria without casts is most frequent in young adults. It is not a symptom always of incipient nephritis but often evidence of lowered resistance and predisposition to infection (tuberculosis). The death rate is higher than among normal subjects (Barringer, Jr., and Warren). It should be remembered that the most severe forms of nephritis are those with but little or no albuminuria and few or no casts (See Casts and Interstitial Nephritis). *The quantitative loss of albumin is not, as a rule, in proportion to the severity of the underlying disease—large loss often offers a better prognosis than does the small trace with evidences of arteriosclerotic disease. Young subjects with albuminuria of indefinite origin are less likely to develop chronic nephritis ultimately than are those beyond twenty-five. At middle life the possibility of nephritis is increased with recurring albuminuria with or without casts.* With casts the diagnosis of nephritis is materially strengthened. We are not referring to cases in which, for instance, in the course of an examination for life insurance, on a single occasion, or during a day or two, transient causes provoked temporary albuminuria, nor to the albuminurias which have resulted from acute poisoning or febrile disturbances, but to those albuminurias for which there seems to be no adequate cause but which recur on slight provocation. *Before any albuminuria can be interpreted as being insignificant, the blood state, the arterial tree and heart, including the blood pressure, demand full consideration. There are functional or so-called physiological albuminurias, but they are exceedingly rare.*

Cyclic Albuminuria.

Orthostatic-Postural Albuminuria

With orthostatic or postural albuminuria the albumin presence is dependent upon changes in the position of the body—the upright posture of the trunk or muscular fatigue.

In these cases the albuminuria is more or less "cyclic." The urine voided before or on arising in the morning is albumin free; after even moderate exercise during the morning hours albumin is present and the loss is likely to be greater during the early afternoon hours, in some cases gradually disappearing toward night.

Nicholson reports "that 7.5 per cent of English school boys among 189 healthy lads studied, showed albumin on arising, 7 per cent after

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breakfast, 10.7 per cent after football, and 18 per cent after a three mile run." Twenty-eight per cent showed albumin at some time. Bugge found orthostatic albuminuria in 14.9 per cent of 1,076 school children in Christiania. Bass and Wessler found "that children with orthostatic albuminuria who showed marked cardiovascular symptoms could not be differentiated by means of blood pressure tests from the remainder of the group."

I have not found orthostatic albuminuria frequent among tuberculous children; some claim that orthostatic albuminuria is usually, if not always, a sign of tuberculous infection somewhere in the body.

Reyher collected 20 cases of orthostatic albuminuria in all of which he found tuberculosis. Arnold does not believe that orthostatic albuminuria is pathognomic of tuberculosis. *Orthostatic albuminuria should always be considered as suggesting tuberculosis but it is not pathognomic.* Sturm found 12 of 20 cases of tuberculosis with orthostatic albuminuria. It is unsafe to conclude that a urine which is albumin free on arising and becomes albuminous and remains so during most of the day, and shows variations in the quantity of albumin, is always an example of cyclic or orthostatic albuminuria. I have under observation at the present time a boy, aet. 12, who was supposed to have an innocent orthostatic albuminuria because of its characteristic cyclic behavior, who now shows renal epithelia and casts, heart and blood pressure changes which are dependent upon tubal nephritis.

Cyclic albuminuria (orthostatic) which may not depend upon serious renal changes in young and growing children (10 to 20 years of age) usually boys, is in most cases nucleo-albumin; in some there may be serum albumin and occasionally both are combined.

Persistent orthostatic albuminuria should be considered to be dependent upon a relative circulatory insufficiency (Crofton).

When so-called "orthostatic albuminuria" continues beyond puberty, though casts may be absent during long periods, organic kidney change should be suspected and such subjects, unless they die of intercurrent disease, finally develop nephritis. Such cases are not true orthostatic albuminurias. The favorable cases of orthostatic albuminuria are without hypertension, accented second aortic sound and hypertrophy, and void the normal quantity of urine without nocturnal urination.

It has been amply demonstrated that *spinal curvature, particularly lumbar curve,* may provoke orthostatic albuminuria which disappears with the correction of the deformity. Erlanger and Hooker found that under such conditions the albumin is excreted during periods of low pulse pressure. Erlanger and Hooker, and Jehle—who has recently published an interesting monograph on albuminuria of lordotic—orthostatic origin—offer a good prognosis when the curvature is amenable to treatment.

I agree with Luthje who says: "I believe that for practical thera-

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peutic purposes it is safest to treat these cases (of persistent orthostatic or cyclic albuminuria) as if they were mild forms of nephritis, at any rate so long as the albuminuria persists; though it is unnecessary to limit the activities of these subjects by interdicting all arduous occupations and the pleasures of life." These conclusions prove that the prognosis is not to be given without reservation in the persistent cases; the possibilities of grave organic disease cannot be ignored. Senator insists on the close relationship of cyclic albuminuria and nephritis, while Huebner acknowledges "a constitutional weakness of the kidney filter" which bears no relation to nephritis.

Albuminuria in the Aged and Young

Albuminuria in the aged and young with occasional casts and without other evidences of advancing nephritis, may persist during many years without final evidences in dropsy, uremia, or circulatory changes of serious disease. Such patients may reach old age or die of intercurrent disease; probably but limited portions of the kidney are involved (*circumscribed nephritis*).

The occasional trace of albumin and few hyaline casts in men beyond fifty has been interpreted by Osler as of "positive advantage." Such men are thereby warned, mend their method of living, prevent further insult to the kidney, and thus prolong their lives.

The persistent presence of albumin in men beyond fifty years of age with or without hyaline or granular casts takes such subjects out of the insurable class.

Febrile Albuminuria

With the separate infections I have fully considered the significance of albuminuria. It cannot be denied that the milder infections are less likely to have albuminuria than are the severer types, but in the majority of bacterial toxemias there is usually more or less albumin excreted, and this runs parallel with the fever. Hayashi holds that "acute infections predispose to alimentary albuminuria," and concludes that "not infrequently in cases of albuminuria there can appear in the urine unchanged albumin from the food ingested." (?)

Febrile albuminuria with non-malignant infections in which the quantity of the urine is not materially reduced and profound toxic symptoms are absent, does not as a rule materially influence the prognosis. Deep toxemia is made more serious by kidney invasion in which there are evidences of toxic nephritis, reduced quantity of urine, abundant albumin, many casts, low urea output, and invasion of the sensorium.

The albuminuria of the first week of *scarlet fever* is in no way related to the acute nephritis which follows the febrile period.

With *cholera*, albuminuria may depend upon nephritis and toxemia;

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in the severe cases anuria and uremia are threatening. If the patient withstands the acute infection the kidney lesion with associated symptomatic albuminuria yields completely, leaving no remnant. The albuminuria and nephritis of pneumonia, epidemic cerebrospinal meningitis, whooping-cough and other acute infections, are not associated with uremia, edema or hypertension, and recover fully if the primary disease does not prove fatal. The same holds true of typhoid fever. The danger in all of these is primarily due to the virulence of the infection and secondarily to the lack of resistance of the patient. The prognosis of *influenza albuminuria* (nephritis) in which there may be large albumin loss, hematuria, and slight hypertension, is good.

With diphtheria and scarlet fever, suddenly arising albuminuria, deep toxemia, scanty urine, and many casts make an unfavorable complex.

With streptococcus tonsillitis, albuminuria may occasionally prove to be the first symptom of a progressive nephritis which remains uninfluenced by treatment. Such behavior is infrequent, but possible. As a rule the slight albuminuria of tonsillar infection yields during the convalescence of the patient. The *malignant infections* which from the beginning offer an unfavorable prognosis, always show albuminuria—usually septic nephritis.

Toxic Albuminuria

Albuminuria due to the poisons has been separately considered (See Intoxications). *Albuminuria following anesthesia*, ether or chloroform, is transient and without danger in normal subjects.

Albuminuria with glycosuria is separately considered (See Diabetes Mellitus); it is always of very serious significance.

Albuminuria associated with the constitutional diseases (the anemias, purpuras, and malignant diseases) is a part of a grave process as a rule; the albumin loss *per se* is not paramount—the albuminuria is but a single symptom of the fatal primary disease.

The albuminuria of pregnancy, not dependent upon nephritis, demands close observation and a guarded prognosis; as a rule it is favorable and transient. The *nephritis of pregnancy* is separately considered (See Nephritis of Pregnancy).

Albuminuria with Functional and Organic Nervous Diseases

I have separately considered the prognostic significance of albuminuria with diseases of the nervous system, not of infectious origin. These include *epilepsy* (during and after convulsions), *delirium tremens, cerebral apoplexy, neurasthenia, migraine,* and at times *hyperthyroidea.* With each of these, differentiation is demanded for in some, there are likely to be arterial and renal changes of organic nature which influence

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prognosis unfavorably. Without such changes as a cause of albuminuria, the latter—usually transitory—is without marked influence.

Sudden albuminuria with intestinal obstruction and promptly developing anuria following in a few hours, is a complex, associated with collapse as a rule, and death.

Albuminuria following surgical operations in those previously albumin free is not infrequent, but always demands close investigation. If due to the anesthetic it promptly disappears; if due to transitory circulatory disturbance it is evanescent; if with casts, lowered secretion, and toxic symptoms—an expression of general infection—the prognosis is unfavorably influenced by the complication. Albuminuria, casts and deep nervous symptoms following operation are always of grave import. Exacerbation of nephritis following operation is infrequent.

For the insurance examiner a conclusion based upon albuminuria *alone* is valueless. Those assuming the risk have learned that the cellular elements in the urine—the presence or absence of casts, at times cylindroids—the general condition, the blood pressure and the condition of the cardiovascular system, the evidences of changes in the fundus of the eye, and the blood picture, are the paramount factors in deciding upon the insurability of the individual.

For further data bearing on the prognosis of albuminuria the reader is referred to the parts of this section dealing with the nephritides and other kidney lesions, as well as the separate diseases of which albuminuria is a symptom. This will lead to the consideration of the circulatory, nervous, digestive, hemopoietic and most other systems, as already suggested in the beginning of this chapter.

While the prognostic importance and seriousness of albuminuria has unquestionably been overestimated in the past, because of faulty diagnostic methods and hasty conclusions, the relative value of the symptom must always rest on thorough differentiation.

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(*b*) *Casts*

Tube Casts

Casts are not always indicative of true nephritis. Casts are frequently found to be transitory and of no pathological significance. Healthy individuals, after excessive exercise, fatigue, or functional disturbance of the kidney, due to improper diet or long continued strain, may show the presence of hyaline casts during only a limited period without further impairment of the general health or permanent kidney change. The persistence of casts—hyaline or granular, or both, with or without albuminuria, should always lead to thorough search and in the majority of cases will be found dependent upon organic disease of the kidney (nephritis). *Promptly disappearing casts* are of no grave importance. The use of salicylic acid preparations and other urinary irritants is often associated or followed by a shower or the presence of casts which may continue one or two days after discontinuance of the drug.

Casts are molds of the renal tubules and when persistently present they are, as a rule, evidence of kidney disease. Their prognostic significance is as easily over- as underestimated, unless the many data which make diagnosis and prognosis positive are gathered from a thorough study of all that the urine offers with a detailed consideration of the other subjective and objective features of the individual case. There are three leading varieties:

1. Blood Casts
2. Epithelial Casts
3. Hyaline Casts.

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Pus casts are simply pus cells plastered on a basement substance, either hyaline or hyaline and epithelial. The *fatty or oily casts* are varieties of epithelial casts which have undergone fatty degeneration. *Waxy or amyloid* casts are like hyaline casts but show the amyloid reaction, are highly refractive, and are characteristic of amyloid disease; they are always secondary and when not specific, are as a rule associated with fatal disease (See Amyloid Nephritis).

Granular casts are degenerated or changed epithelial casts. *Cylindroids* are composed largely of mucus with added elements held together by a basement substance. They are formed in the tubule or at times in the pelvis of the kidney and are expressive of more or less irritation of the part in which they are formed; they are less serious than are casts and are often dependent upon transitory causes, though they may be found with other casts in the more serious organic diseases of the parenchyma of the kidney.

1. Blood Casts

Blood casts show the seat of existing hemorrhage to be in the tubules of the kidney, including the glomeruli. When the microscope shows the presence of blood casts, the prognostic significance must depend upon a number of factors, the most important of which include the nature of the primary lesion which has caused the bleeding. *In young subjects* tuberculosis, calculosis, occasionally malignant growths and acute nephritis, are among the leading causes (See Hematuria). *During middle life* tuberculosis, calculosis, malignancy, renal and circulatory disturbances (secondary to heart, vascular, and liver disease) are among the underlying anomalies. *In advanced life*, arteriosclerotic, cardiovascular disease, nephritis, varicosities, malignancy (cancer and papilloma) calculosis, and other causes are among the possibilities. The blood casts of acute nephritis in young subjects are often abundant (scarlatinal nephritis, etc.). The prognosis is not bad so long as profound uremia is prevented and the associated conditions are not threatening.

Blood casts in young subjects with anuria and uremic symptoms are always ominous and demand a guarded prognosis. The prognosis is not necessarily unfavorable in cases which appear serious and threatening under rigorous and rational treatment (See Acute Nephritis). The length of the threatening period is short in the majority of these cases. An occasional blood cast in adult nephritis is not of serious moment. Often with acute exacerbations the urine of subacute and chronic nephritics may become bloody—in the majority it clears after a few days of rest and treatment. Occasionally the presence of a few blood cells and blood casts precedes a free hemorrhage and serious uremic symptoms.

2. Epithelial Casts

Epithelial cells plastered on a hyaline basement substance are char-

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acteristic of acute tubal nephritis. Epithelial casts are positive evidence of tubular involvement; considered alone they offer little of prognostic value, their diagnostic significance is more important. Abundant epithelial cells and casts with progressive reduction of the urine secretion, with or without blood casts or blood corpuscles, with dropsy and increasing nervous symptoms are always ominous, though not of necessity fatal (See Acute Nephritis).

When epithelial casts become fatty and granular they indicate a degenerative process, characteristic of the more advanced forms of nephritis. The persistence or even occasional presence of epithelial casts with albuminuria, with at times the addition of a hyaline cast, in a urine which shows progressive lowering of its specific gravity, is indicative of either secondary contraction of the kidney following tubal nephritis or chronic interstitial nephritis, and the prognosis should be accordingly given (See Chronic Tubal Nephritis and Interstitial Nephritis).

It is an established fact that subjects with granular casts and albuminuria are bad risks, and show a mortality far above that of the normal individual. They are below par and yield to infection readily when exposed. The more acute the nephritis, the better is the epithelium preserved; hence degenerated epithelium as plastered upon hyaline substance to form granular and fatty casts is always an expression of advanced tubular change.

3. Hyaline Casts

Hyaline casts are homogeneous, glassy, are regularly outlined, and are *not highly refractile, in contradistinction to waxy casts which are highly refractile.*

I considered the association of an occasional hyaline cast with moderate or transitory albuminuria in men beyond fifty years of age (see Albuminuria) and called attention to the salutary influence of such occurrence (Osler). The diagnostic and prognostic significance of hyaline casts with or without albuminuria depends upon age, associated conditions, and a variety of factors which are numerous in individual cases. Hasty conclusions in the presence of hyaline casts and albuminuria are likely to prove erroneous and expensive. *Hyaline casts may be found occasionally in the urine of normal subjects; persistent albuminuria with hyaline casts and an occasional granular cast indicates nephritis, and the forecast should be accordingly given. An occasional hyaline cast with albuminuria after excitement, exertion, overeating does not necessarily mean diseased kidney.*

When albumin is present on arising in the morning in large or small quantities with hyaline casts—many or few—but one safe conclusion is justified, and that is that we are dealing with an abnormal condition which demands the close study of the patient before reaching a conclusion;

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further, it should be remembered that hyaline casts may be present with all forms of nephritis, with jaundice, diabetes mellitus, and insipidus, heart lesions, pregnancy, and after long walks or marches (soldiers) with gouty exacerbations and under various conditions which are especially influenced by excitement, mental emotion, and diet.

My experience coincides with that of Barringer, Jr., and Warren who assert that "cases of albuminuria with a few hyaline casts have no particular age incidence. The mortality of this group is also above the normal."

The prognosis of *febrile albuminuria, toxic albuminuria, and all forms of albuminuria due to infection with the presence of casts* depends upon many factors which are considered in connection with the separate diseases (See Section I—The Infections). It may be safely assumed that deep kidney involvement—with or without casts complicating acute or chronic disease—always adds an enormous element of danger (See also Cardio-vascular Disease, Arteriosclerosis, etc.).

Hyaline casts with congested kidney and blood casts, an occasional granular cast, scanty urine, and clouded sensorium are among the terminal features when compensation is broken, usually beyond repair. Casts often precede albuminuria during the early days of acute nephritis (Pick, Hecht and Koessler). *The gravest types of nephritis may remain without demonstrable casts during weeks and months* (See Interstitial Nephritis; also Secondary Contracted Kidney).

In the presence of any form of nephritis with acute exacerbation, the gravity is often in direct proportion to the profusion of the urinary casts though there are abundant cases in which the number of urinary casts is in no way related to the gravity of the disease. Grave and threatening nephritis—often in the terminal stages—may show but few or no casts, but little or no albuminuria; chronic nephritis (usually interstitial) may remain "albumin and cast free" during days or months at a time, when suddenly symptoms of toxemia develop, uremia without warning, coma and death.

Fischer after considering the mode of formation of casts, basing his conclusions upon the influence of acid, etc., says: "These simple facts regarding the origin of casts, and the conditions under which the one type may be converted into another, are not without some clinical significance." . . . "It seems to me that the experiments that have just been detailed urge upon one the necessity of caution in drawing sweeping conclusions from such data. So far as mere numbers of casts are concerned, it requires no special emphasis to realize that great numbers of casts present in the urine at one time, while indicative of a more extensive involvement of the kidney parenchyma, may not be as significant as a lesser number present over long periods of time. The aggregate destruction may in the latter case, of course, be much greater than in the

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former (a condition further modified in the living organism by the rate and quantity of the regeneration occurring in the kidney)."

With septic and embolic nephritis, pyelonephritis, and other deep infections involving the kidney, *bacterial casts* are found in the urine composed of agglutinated masses of bacteria in the freshly voided urine. The presence of these masses of bacteria, probably agglutinated in the kidney, is one of many serious features of grave infection. Neubauer and Huppert and others call attention to the importance of examining the urine immediately upon its passage; otherwise the clinician may be deceived by the formation of conglomerate masses of bacteria into forms which resemble the renal bacterial casts.

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(c) *Hematuria*

Origin.—Visible blood in the urine—the symptom hematuria—may be either of *renal* or *extra-renal* origin. The determination of the cause of hematuria is often difficult because the bleeding may be without subjective symptoms or physical signs.

Cystoscopic examination with catheterization of the ureters makes the localization of lesions more positive than ever before, though the majority of hematurias will for many years to come be diagnosticated by the average clinician without the aid of these refinements of diagnosis. Whenever possible, advantage should be taken of this new method of diagnosis. The methods suggested make possible the localization of lesions to one or both kidneys in renal hematuria but they fail in many cases to establish the true underlying pathologic condition. For prognosis and diagnosis it is fortunate that the overwhelming number of hematurias find their way to the diagnostician early, for blood in the urine rarely fails to alarm the patient who usually demands immediate treatment of the symptom.

Blood may enter the urine from any one of many sources; beginning

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with the malpighian tufts and ending with the meatus urinarius, there is not a surface which when disturbed may not add blood elements to the urine. Besides local lesions within the urogenital tract, hematuria may complicate the *constitutional diseases with hemolysis* when it is but one symptom of a grave and usually fatal malady. With grave local (renal) or constitutional diseases there are besides the hematuria, sufficient subjective and objective features to clear the diagnostic horizon and to lead to a safe forecast.

There are but few conditions associated with hematuria in which the bleeding is so profuse (this is particularly true of bleeding from the kidney) as to threaten life. It does occasionallly happen that hematuria is profuse and depleting. Many cases become excessively anemic, but few of these die as the direct result of the hemorrhage. In the terminal stages of malignant disease of the kidney or bladder, at times with malignant purpura, pernicious anemia, Hodgkin's disease, or with hemolysis due to other grave constitutional diseases, the bleeding may so weaken the patient as to add an enormous element of danger (See also Malignant Jaundice and other grave liver infections).

Renal hematuria is more frequent than is generally supposed without analyzing a large number of cases. The symptom may be continuous, or it may recur at irregular intervals. Hematuria due to organic change in the kidney which is permanent is likely to recur, and it is unwise for the physician or patient to believe that the organic disturbance has been overcome because of periods of latency or the insidious behavior of the underlying process, which adds but little to the clinical history during long periods. This sense of security after kidney hemorrhage even without associated symptoms, sufficient to make its cause positive, is rarely justified, for it may be assumed that the bleeding must always be considered an important symptom, demanding close surveillance during many months and years; such conclusion and consecutive action will do much to improve prognosis.

I have in private practice tabulated the clinical histories of 4,832 consecutively examined cases of internal disease. I found among this number 229 cases of chronic tubal nephritis, 14 cases of acute tubal nephritis, 77 cases of chronic interstitial nephritis, 8 cases of secondary congested kidney with the prominent symptoms of marked stasis, and 7 cases of tuberculous nephritis, in which no tuberculosis was demonstrable in other organs. Of the 229 cases of tubal nephritis, blood was found in the urine of 33 per cent. The 14 cases of acute nephritis all contained more or less blood. Of the 77 cases of chronic interstitial nephritis 14 per cent were found with blood in the urine. All of the 8 cases of secondary congested kidney contained blood. In only 12 of the 328 cases, was the hematuria profuse. In 4 of these there was chronic tubal nephritis with marked hypertension, arteriosclerosis and aortic disease, with, in one case,

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a final malignant growth in the bladder. In 4 of the 12 profuse hemorrhages there were evidences of gouty kidney with advanced interstitial change. The remaining 4 cases showed microscopic elements which justified the diagnosis of chronic tubal nephritis.

Rayer in 1844 called attention to the frequency of nephritis as a cause of hematuria, and Askanazy presents the results of the observation of 562 cases of chronic nephritis, 35 per cent of which showed blood in the urine. Of these 126 showed moderate, 64 abundant red corpuscles. It is evident from the foregoing statistics that while bloody urine is a frequent symptom of all forms of nephritis—tubal nephritis particularly—it is rarely threatening or profuse.

Hematuria may be a Symptom of:

1. Acute Tubal Nephritis
   (Hemorrhagic (acute) Nephritis)
2. Chronic Tubal Nephritis
   (a) painful
   (b) painless
3. Chronic Interstitial Nephritis
   (Hematuria due to arteriosclerosis, change in blood pressure and localized degeneration)
4. So-called "Essential Hematuria" or "Renal Epistaxis"
5. Cases of Renal Hematuria with gouty diathesis in which there may be latent kidney disease without calculosis
6. Paroxysmal Renal Hematuria following chilling of the surface
7. Renal Infarct causing hematuria with septic fever, usually associated malignant endocarditis
8. Acute and Chronic Primary Infections—pyelitis, non-calculous, with moderate hematuria.
9. Stone in the Kidney
10. Tuberculous Nephritis
11. New Growths of the Kidney
12. Traumatism causing rupture of the kidney
13. Echinococcus
    Bilharzia Hematobia
    Filaria Sanguinis Hominis
14. Constitutional Diseases
    (Purpura and the Anemias)
15. Hemorrhagic Conditions with the Infections—scarlet fever, typhoid and typhus fever, measles, smallpox and diphtheria and following surgical operations

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1. *Acute Tubal Nephritis*

These cases are easily recognized: the urinary (microscopic) picture is characteristic in the preponderance of cellular elements, the hemorrhage is rarely profuse, blood in small quantity is usually present, in the hemorrhagic form bleeding may be profuse with other serious symptoms, including scanty urine and uremia. Hematuria with acute nephritis is rarely of serious importance.

2. *Chronic Tubal Nephritis*

The hemorrhage may be (a) painful or (b) painless. It is rarely sufficiently profuse to materially add to the dangers of the case; in occasional cases with acute exacerbation of the already existing chronic nephritis the urine may show considerable admixture of blood. Most uncomplicated cases are painless. The prognostic significance of hematuria with chronic tubal nephritis (uncomplicated) is not great. The process in the kidney is progressive and disseminated, of constitutional origin, and is not materially influenced by the hemorrhage. With chronic tubal nephritis but one kidney may bleed, though both organs are equally invaded; both may bleed at the same time or they may alternate in adding blood to the urine (For further data see Chronic Tubal Nephritis). *In this form of nephritis as in all others, the general condition of the patient, his resistance, the blood state, blood pressure, specific gravity of the urine, as well as the functional ability of the kidney, demand consideration, that a safe forecast may be given when hematuria is a prominent symptom.*

3. *Chronic Interstitial Nephritis*

Included is a class of hematurias in which there are advanced arterial lesions, the blood pressure is abnormally high, and there are localized degenerative changes—particularly in the walls of the arteries, at times in the veins—with possible rhexis. In these cases the hematuria, *per se*, is not threatening; active exercise or faulty diet, excitement, or emotion may cause relapse; chronic constipation aggravates or provokes the bleeding (straining at stool).

In some of these cases there may be hemorrhage from other sources, as the urethra, bladder or pelvis, and it not infrequently happens that cerebral hemorrhage ends the life of such nephritics. In one of my cases observed during many years, the original hemorrhage was profuse and from the urethra, the second from the nasal mucosa, the third from the kidney. Death followed from cerebral hemorrhage after a fishing trip on a hot summer day. In these cases hematuria may occur in conjunction with transitory hemiplegia.

In offering the prognosis of these cases the possibility of the complica-

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tions suggested should be considered and the further fact remembered that *profuse renal hemorrhage with chronic interstitial nephritis is more frequently due to changes in the pelvis of the kidney than to any other single cause;* that the blood vessels may either rupture here or that there may be a sudden hyperemia, such as surgeons have found during surgical operations upon the kidney (Israel) and that as in the brain, increased arterial tension is an important factor in causing rupture of diseased arteries or veins (Elsner).

4. *So-called "Essential Hematuria" or "Renal Epistaxis"*

So-called "essential hematuria" or "renal epistaxis" is supposed to exist without organic change. Well authenticated cases are so rare as to cast doubt upon the correctness of this conclusion. Several years ago I reviewed the literature of this subject and found but few well authenticated cases (Klemperer, Senator, Schede, Caspar, and Schenck). The kidneys in the cases of Klemperer, Schede, and Schenck were found normal after nephrectomy. Caspar reports 7 cases of so-called essential renal hematuria, or as he says "bleeding from healthy kidneys." The consideration of his material strengthens him in the conclusion that the majority of these mysterious cases are due to nephritis, though clinical manifestations may be entirely absent. In this connection, for purposes of prognosis, it should be remembered that *nephritis may persist during many months without casts or albumin, and during long periods without hemorrhage.*

Schenck's case in which the cause of the hemorrhage after the removal of the kidney remained a complete mystery led him to conclude that it would seem far better to put these cases aside as yet unexplained, than to assert that an anatomically sound kidney could cause profuse hematuria. *The majority of cases which are originally diagnosticated as "essential hematuria" prove ultimately to be either chronic, tubal, or interstitial nephritis with limited or punctiform change in the substance of the organ or its pelvis, often undiscoverable macroscopically but usually demonstrable microscopically.*

In a number of cases the final history leaves no room for doubt because of the development of the complete clinical history of nephritis. When the hemorrhages are profuse and recur at short intervals, *secondary anemia* may prove serious, and when the process is limited to one kidney (as shown by ureteral catheterization) surgical intervention may be needed to save life.

Unexplained and supposed *"renal epistaxis"* may be slight and never recur—may leave no remnant of renal change. The pain is rarely severe; some cases are painless.

The prognosis in the majority of cases, of the symptom itself is good

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(Hale White). Probably the hematuria of pregnancy is due to varices of the renal pelvis. The prognosis is good.

5. *Cases of Renal Hematuria with Gouty Diathesis in Which There May Be Latent Kidney Diseases without Calculosis*

These cases usually advance after a number of years and show all of the changes of chronic interstitial nephritis, at times secondary contracted kidney. The hematuria does not materially interfere with the course of the disease in the majority of cases, though occasionally the progression dates from the bleeding. With acute exacerbation of gout in nephritics, hematuria may be a prominent symptom. The majority of these cases yield to rest and treatment. In occasional cases profuse hematuria associated with the gouty diathesis may be the first of a long train of symptoms which characterize chronic interstitial nephritis.

6. *Paroxysmal Hematuria following Chilling of the Surface*

The history of these cases is interesting. Usually the patient is a middle aged man, who had considered himself perfectly well; he is exposed to cold, a slight chill follows, with a desire to urinate. The urine is bloody at once and is voided without pain. The hematuria is profuse and continues during twelve to twenty-four hours, to return whenever there has been exposure to cold. Usually these patients complain of cold feet before the chill and hemorrhage. During the summer months there are no renal hemorrhages. Finally the hematuria recurs on slight cause, evidences of nephritis (chronic tubal) are continuous, and death with all of the symptoms of chronic nephritis, usually dropsy and uremia, with cardiovascular change follows. These cases may prove exceedingly chronic. One of my cases lived over 17 years after the first hematuria. He died of uremia preceded by a long period of renal dropsy.

7. *Renal Infarct Causing Hematuria with Septic Fever, Usually Associated Malignant Endocarditis*

A strong suspicion of malignant endocarditis and renal infarct is justified when there is associated septic or pyemic fever (intermittent fever) in which there is no other clear cause for the bleeding. Renal hematuria may be an early or a late complication of infectious endocarditis. I have seen chronic malignant (Streptococcus viridans) endocarditis uninfluenced by the early renal infarct; as a rule, there is recurrence, with evidences of infarct in other organs (spleen, brain, lung, and skin). In one case hematuria recurred at varying intervals during six months preceding death. Hematuria is not the cause of death. The infection is malignant,

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often chronic, and always offers a bad prognosis. I have no recovery to report (See Malignant Endocarditis).

8. *Acute and Chronic Primary Infections—Non-calculous Pyelitis with Moderate Hematuria*

These are the acute cases of primary infection of the pelvis of the kidney, in contradistinction to calculous pyelitis or ascending pyelitis due to gonococcus or other infection. There is a characteristic history, including temperature curve, most frequently found in women—often during pregnancy and at the menstrual period.

The renal pelvis is directly infected, usually by the Bacillus coli commune, occasionally by other pathologic bacteria—pneumococci, paratyphoid bacilli, etc. Obstinate constipation is usual; bladder symptoms are absent. The temperature following the direct (non-ascending) infection is almost pathognomonic; high at first during from three to four days, then a period of remission, almost normal temperature for two to four days, then a series of chills and intermittent fever. These cases may be subacute or chronic—eight to fourteen days—some several weeks, others continue a number of months. The disease is usually right-sided; in thin subjects the kidney is palpable, tender and enlarged (Elsner). The sharp pains resemble renal colic; they radiate along the ureter; the hemorrhage is not often profuse. Lenhartz's résumé of the subject is classic.

My experience with these cases, without surgical intervention, has been favorable. Often the anemia becomes extreme. In those complicating pregnancy, the fever and local symptoms of infection and anemia usually disappear after delivery—recovery is complete as a rule.

9. *Stone in the Kidney*

Renal calculosis does not, as a rule, cause profuse hematuria. I have never met a case in which hematuria with calculous pyelitis threatened life in an otherwise healthy subject. The prognosis of kidney stone is separately considered (See Pyelitis Calculosa—Kidney Calculosis).

10. *Tuberculous Nephritis*

(See Tuberculosis of the Kidney—Section I)

Most hematurias due to tuberculous disease of the kidney are finally controlled; I have never experienced death from hematuria *per se.*

Hematuria with tuberculous nephritis is often the first symptom of renal infection. My experience does not include many cases of profuse hematuria after the tuberculous process was far advanced. With radical treatment the prognosis in threatening cases is good. *The early recogni-*

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tion of the pathologic cause of the hematuria in tuberculous nephritis and prompt surgical treatment offers an excellent outlook for the complete restoration to health in cases in which the process is not disseminated or double.

11. *New Growths of the Kidney*

(See Neoplasms of the Kidney)

Early hemorrhage with cancer—papilloma of the kidney or other renal growths, when the cause is clear and radical treatment not too long postponed, offers a good prognosis.

12. *Traumatism—Rupture of the Kidney*

In otherwise healthy subjects without injury of other organs and prompt surgical treatment, the prognosis is relatively good. There are naturally many factors associated with the accident which influence the outcome, but it may be safely concluded that unless the ruptured kidney is surgically treated the prognosis is absolutely bad in practically all cases. There are but few exceptions.

13. *Echinococcus Disease, Bilharzia hematobia, Filaria sanguinis hominis*

(See Section I—Parasitic Diseases, etc.)

14. *Constitutional Diseases*

(*Purpura, Hemorrhagic Diathesis, the Anemias, Hemophilia, etc.*)

(See separate chapters dealing with individual primary diseases)

Hematuria, petechiae and other evidences of the hemorrhagic diathesis with constitutional disease, are usually terminal. The prognosis of the primary disease is of paramount importance in reaching a safe conclusion. With *purpura* (uncomplicated and benign) the prognosis is good. With the other constitutional diseases, *pernicious anemia, Hodgkin's disease,* the *leukemias,* the prognosis is always bad.

15. *Hemorrhagic Conditions with the Infections*

(*Scarlet Fever, Typhoid and Typhus Fevers, Measles, Smallpox, Diphtheria and following Surgical Operations*)

We have separately considered hematuria and the hemorrhagic complications of the infections. They are always of serious significance, always evidence of malignancy of the primary infection, and often fatal.

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Hematuria is usually but one symptom of the complicating diathesis and profound constitutional disturbances. *Following major surgical operations* the hemorrhagic symptoms are, as a rule, evidence of grave infection and are always discouraging. With *measles,* hematuria may not always prove to be a serious complication—it is often transitory and may leave no remnant of kidney change.

Hemoglobinuria

The presence of hemoglobin or methemoglobin in the urine is evidence of a primary hemoglobinemia and hemolysis, in which the destruction of red blood corpuscles has been extensive. *Toxic hemoglobinuria* may follow the ingestion of a number of poisons including potassium chlorate, arsenic, antimony, toluylendiamin, nitrobenzol, quinin, turpentine, carbolic acid, lysol, the anilin dyes, carbon monoxid and muscarin.

In severe cases of infection—scarlet, typhoid, typhus, streptococcus infection—hemoglobinuria is an expression of blood destruction and malignancy. I have seen hemoglobinuria after transfusion of blood and large surface burns. With the latter it is always ominous, usually fatal.

Periodic hemoglobinuria is usually a chronic recurring condition which follows exposure to cold in susceptible individuals, usually males. As a rule if these patients escape without cold feet, hemoglobinuria is prevented, but in most cases exposure to cold and cold extremities promptly cause the symptom. In occasional cases of Raynaud's disease during the winter months, *paroxysmal hemoglobinuria* is an annoying symptom. Osler reports one case in which his patient with Raynaud's disease had paroxysmal hemoglobinuria and epileptic seizures at the same time.

The prognosis of the toxic form of the symptom depends upon the constitutional effect of the poison; with the infections it is always grave. *The prognosis of paroxysmal hemoglobinuria is favorably influenced by climatic treatment.* I know of no fatal case directly due to the complication. One chronic case finally died of chronic tubal nephritis and uremia.

Recent studies of the blood serum of these patients prove the presence of a powerful toxin which causes the destruction of the erythrocytes. There is an "amboceptor component of the hemolysin" which at a low temperature in the presence of the complement unites with the erythrocyte and by autohemolysis dissolves the cells themselves. When due to syphilis, radical treatment may bring relief.

Spontaneous cures are recorded. The *duration of the separate attack varies from a few hours to several days.*

The graver attacks may include hemolytic jaundice, striking anemia, muscular enfeeblement and finally splenomegaly.

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(*d*) *Uremia*

Uremia, whatever theory we finally adopt to explain its production, is always evidence of faulty metabolism and auto-intoxication dependent upon the reduced functional ability of the kidney. It is a true poisoning in which blood changes are practically constant and the associated or consecutive symptoms are never to be lightly regarded. When acute, they are often life-threatening; when subacute or chronic and not overwhelming, they are often borne for long periods during which the clinical picture may vary from time to time, the toxemia may yield, the central nervous system may resume its normal functions and the gastro-intestinal discomfort and cardiac complaints may disappear entirely if the primary cause has been removed. Relapse, with chronic kidney disease may be expected at any time.

Uremia as a rule is more grave in direct proportion to the extent of the kidney lesion and the disorganization or degeneration of the organ. In the presence of disorganization or destruction of kidney tissue, it is certain that the functional ability of the organ is reduced, but besides this, it is probably equally true that a *nephrolysin* (a poison) is elaborated. In consequence secondary changes including toxemia (uremia), increased blood pressure, and nervous as well as gastro-intestinal symptoms promptly develop.

Uremia is a symptom complex. The leading features include reduced kidney function, disturbances of the nervous and digestive systems. Whenever there are evidences of uremia, for diagnostic, prognostic, as well as therapeutic purposes, in the light of our present knowledge, the safest

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conclusion to reach is that the symptoms are of toxic origin, that the blood stream is surcharged with effete matter (urea), and that the patient is never out of danger until the quantity and quality of the urine are within safe limits. See References for Armard Formula and importance of the increased urea content in the blood, also Renal Sufficiency tests. *Every acute or chronic nephritic who develops nervous symptoms or who has gastro-intestinal disturbance which can be explained in no other way,* should be *considered uremic until proved otherwise.* With *acute nephritis* reduction in the quantity of urine, with specific gravity suggesting retention, the microscopic field often rich in casts and blood elements, the urine frequently concentrated and smoky, the onset of uremia is to be feared and treatment should be accordingly framed.

Uremia may be (I) *acute,* (II) *latent,* or (III) *chronic.* It may present a variety of clinical pictures because of the character and extent of the lesions, the resistance and idiosyncracies of the patient. The leading features upon which prognosis is founded are referable to the nervous, the cardiovascular and renal system, the stage of the disease and the extent of consecutive changes in the many organs, often invaded.

I. Acute Uremia

Acute uremia is always an expression of serious renal insufficiency. The prognosis of acute and overpowering uremia is less favorable than is that of most other forms, for as a rule the underlying kidney changes are likely to be serious, the nervous system is profoundly involved, the symptoms are often apoplectiform, the mania may be active and promptly weakening, the gastro-intestinal tract intolerant, and the cardiovascular system not able to carry the patient beyond the critical period.

In spite of these threatening symptoms the prognosis of acute uremia ought not to be made without considering the possibility of relief unless the parenchyma of the kidney is too far advanced in disease or renal function cannot be stimulated. Uremic symptoms may be acute and exceedingly grave and yet—particularly in children with acute nephritis—rigorous treatment may often lead to recovery.

With acute uremia the freer the subject is of cardiovascular changes the more acute the renal changes, and the more these are limited to the parenchyma the better is the prognosis. In some cases *renal sufficiency tests* give some assistance, but alone they are not dependable for in the presence of grave uremia I have found high readings, and vice versa.

Acute uremia with the chronic nephropathies in which there has been a period of latent or chronic uremia does not offer an encouraging forecast. Even these cases are often amenable to treatment and may return to their former state. *Chronic arteriosclerotic nephritics often have long periods of acute exacerbations of uremia, with profound involvement of the sensorium between which they may continue with the chronic tox-*

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emia, or they may clear mentally and return to their responsible positions with average judgment. Relapse in these cases is the rule. The acute exacerbations are repeated, or after a number of these, the uremia becomes continuous and chronic, finally leading to coma and death. Other complications (cerebral apoplexy, cardiac insufficiency, etc.) may also cause the death of these patients.

The increase of urine, and the improvement of the gastro-intestinal symptoms as the brain clears, are favorable.

Sudden blindness just before a uremic convulsion, with acute uremia, is not as a rule evidence of retinal hemorrhage. In my experience the majority of such amauroses have not recurred.

The persistence of vomiting and other gastro-intestinal symptoms after the acute manifestations yield, are not favorable. *Such patients are likely to have convulsions, or because of the profound renal insufficiency they develop chronic uremia. Persistent or recurring drowsiness* after an acute uremic convulsion, with either acute or chronic nephritis is proof of continuous toxemia and is unfavorable though relief is not uncommon after rigorous dietetic treatment and rest.

Acute uremia with respiratory paralysis or irregular breathing—Cheyne-Stokes particularly—with *chronic nephritis* and *arteriosclerosis* is always dangerous.

Pulmonary edema with acute uremia is often a fatal complication. This is not always true for in hospital practice with acute nephritis, acute uremia and pulmonary edema, results have at times been surprisingly favorable.

Abnormally high temperature with acute uremia and cerebral symptoms are unfavorable and suggestive of *meningitis.*

Active mania may be a manifestation of acute uremia. With myocardial insufficiency it is serious; with advanced nephritis it is a grave complication; with alcoholics and nephritis, pneumonia often complicates and usually death results. Mania may follow the acute convulsion or it may develop suddenly without preceding nervous manifestations. The *monoplegias* which follow acute uremic convulsions are at times due to *localized edema of the brain* and yield in the course of a few hours or days.

Hemiplegia is more likely to be due to rhexis of a cerebral vessel and does not offer the same favorable prognosis for restitution of motion as does the more limited paralysis. *Cerebral paralyses of uremic origin* are often exceedingly puzzling, and early prognosis is not always possible for the paralysis may be thrombotic, apoplectic, edematous, or of toxic origin and the prompt recognition of the true cause is impossible.

Batty Shaw has recently written extensively on this subject and I quote from his article: "Turning now to the practical side of the question it is this; that we must not only think of a thrombotic hemiplegia in future, with all the elements of a wrong prognosis following in its wake,

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if we find hemiplegia occurring in a case of uremia or hypertension."—"We may say that the patient may get quite well of the hemiplegia, but we cannot say for certain. The same may be said of cases of recurrent loss of consciousness associated with uremia or hypertension."—"What, then, is the explanation of such curious paralyses? They are almost certainly of toxic origin, and the toxin picks out motor areas in one individual and sensory areas in another."—"The presence of a toxic 'pressor' body, which appears to be so often the case in uremia, makes it easy to understand that such a body acting on the brain vessels would cause them to contract. If the arteries going to the particular area of the brain affected are small, then a moderate contraction of them will produce a relatively greater anemia of such parts than of other parts of the brain, and they suffer to the exclusion of the others."

Extreme dyspnea is always an unfavorable complication of any form of uremia. *Acute uremic dyspnea* without convulsions or other evidences of uremia is occasionally the only symptom; if relieved, when due to chronic nephropathy, it is likely to recur. With marked cardiovascular lesions it offers a gloomy outlook.

Chronic nephritics with severe headaches and acute uremia usually have high blood pressure, secondary changes in the heart and cerebral arteries, and present a train of unfavorable symptoms in connection with the uremia and urine characteristics of disseminated renal disease.

Acute uremic diarrhea with either chronic or acute nephritis in the absence of threatening symptoms, is not as a rule of serious import. Patients are often relieved of annoying nervous and gastric symptoms after this depletion.

Acute uremia in which the patient, immediately following the early symptoms, falls into the "typhoid state" is always grave and demands a guarded prognosis.

Retinal hemorrhages preceding any form of uremia "acute or chronic" are evidences of advanced arteriosclerosis and nephritis, and offer an unfavorable outlook for recovery.

Hypertension long present with nephritis and final acute or chronic uremia is always proof of a grave primary lesion.

A persistently rapid pulse, arhythmia, angina or other evidences of vascular spasm either before or after acute uremia, are unfavorable; most of these patients die within a limited time. Chronic nephropathies which have had one or more acute exacerbations of symptoms, including deep uremia always stand on the edge of a precipice—they may fall without a moment's warning.

II. Latent Uremia

Anuria in the absence of nephritis may or may not give rise to uremia unless relieved within a reasonable time. *Anuria with kidney lesions* is

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likely to be associated with uremic symptoms. *Anuria with some forms of obstruction,* or even with kidney lesions, may persist during several days without marked—at times without any—evidences of uremia; finally there are convulsions or uncontrollable vomiting, increasing heart weakness, air hunger and, unless the obstruction is relieved, death follows.

Anuria due to non-obstructive suppression of the kidney function leads to death in most cases unless relieved in from three to five days; patients with *anuria due to obstruction of the ureter or kidney pelvis by stone,* growth, or other cause may live with but few symptoms as long as two weeks.

With complete suppression of urine, without advanced or chronic kidney lesions, with obstruction to the *outflow of urine due to stones in both ureters or other causes,* I have seen life prolonged during periods of surprising length. In one of my cases (an old man) both ureters were plugged with stones. The patient lived two weeks without secreting urine, never had a uremic convulsion, vomited during the last few days of his life and died without uremic dyspnea.

In children with nephritis, usually *scarlatinal anuria* may persist during three or four days—in some cases without marked evidences of uremia—and recovery, in my experiences, from such complication has been the rule.

I have seen one case of renal sarcoma (a woman thirty years of age) removed surgically, which proved to be horseshoe shaped and her only kidney, in which death followed on the thirteenth day. There are recorded cases in which recovery followed long periods—comparatively speaking—of anuria without marked uremic symptoms or in some with uremic manifestations in the absence of grave kidney change (the anuria usually dependent upon obstruction); the issue has been favorable.

Latent uremia is to be expected in most forms of obstructive anuria. Latent uremia with complete obstruction will finally lead to death unless such obstruction is removed. The condition is usually surgical.

III. Chronic Uremia

There are patients who are really suffering from chronic uremia, who are surcharged with urea and the products of faulty metabolism, who are without annoying or noticeable subjective symptoms but whose urines constantly give evidence of faulty elimination and advanced renal destruction. When these cases are thoroughly studied they prove the correctness of the preceding statement, for they are really chronic invalids; they have persistent indigestion, ocular disturbances, morning headaches; they have a pasty complexion, are always below par and many are with mental processes which are slow and not always dependable.

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This chronic uremia, for that is what these symptoms mean, may suddenly light into an acute exacerbation, or the free and frank expression of the toxic condition may never develop. Most cases, however, either fall into a state in which there are continuous symptoms, or they develop acute uremia unless they die of intercurrent disease. All of the symptoms of acute uremia may be present with the chronic form though less stormy. From the preceding paragraphs it is clearly evident that it is often exceedingly difficult to determine the exact time when chronic uremia commenced.

Chronic uremia may be diagnosticated in the presence of symptoms referable to the nervous system or digestive tract when there are evidences of nephritis and no other cause for the persistent complaints. Occasional deep nervous symptoms, loss of consciousness, uremic dyspnea, transitory amaurosis, sudden emesis with associated cardiac weakness, may recur during varying periods. In most of these cases the evidences of chronic nephritis are positive in cardiovascular and urinary changes (also hypertension) and once established, such deep chronic uremia is not likely to yield, though it may persist during many months.

In both acute and chronic uremia *wakefulness* is often one of the leading symptoms of the toxemia. When with insomnia there is great unrest and a rapid pulse or evidences of cardiac arteriosclerosis (Stokes-Adams phenomenon, coronary symptoms), or the unrest and insomnia are associated with eye symptoms, convulsions may follow or after a number of days the patient, exhausted, falls into a coma, respiratory symptoms follow and but few escape death. It is the exception for patients with any form of chronic nephritis to rally after a considerable period of insomnia followed by convulsions or coma. Children and young adults with acute nephritis may often suffer from sleeplessness during uremia without falling into convulsions or coma. Much depends upon the associated symptoms and stage of the disease in all cases of uremia with insomnia and unrest. With associated occasional delirium or *visual anomalies* the prognosis is not encouraging though not necessarily fatal.

With *non-albuminuric chronic nephritis,* chronic uremia may be present and prove a determining factor in causing death.

Repeated renal or cardiorenal asthma is often of uremic origin and is always serious.

The uremic breath, with many or few symptoms, is always a warning and in most cases general improvement follows its disappearance. The uremic breath with chronic nephritis often precedes acute exacerbation of symptoms. *Convulsions arising suddenly in the course of chronic uremia are always grave.*

With chronic uremia, *skin lesions* (pruritus, etc.) prove rebellious to treatment.

Subnormal temperature is an occasional ominous symptom. *Eleva-*

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tion of temperature above normal is never found in uncomplicated cases of chronic uremia.

Bradycardia with other evidences of heart block and uremia is positively unfavorable. Chronic uremia dependent upon renal lesions, which are also chronic, offers but scant hope of relief. There are chronic nephritics who live during many years with positive evidence of one or more symptoms of chronic uremia; these include headache, occasional vomiting, transitory visual disturbances, anorexia, pruritus, and insomnia. In such cases the prognosis depends upon possible complications of the nephritis, acute exacerbations of uremia, sudden vascular ruptures, heart insufficiency and a variety of complications which are included in the study of the chronic nephropathies. These patients are always between Scylla and Charybdis; ultimately they must strike the rocks.

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(e) *Renal Sufficiency Tests*

The clinician will never be limited to any one test or symptom for the diagnosis or prognosis of the nephropathies or other organic diseases of the kidney. It will never be safe to pin our faith to renal sufficiency tests alone for the prognosis of urogenital disease. Unwarranted enthusiasm has unquestionably led some observers to place too great reliance upon the renal sufficiency tests to the exclusion of other features of paramount importance. Rational diagnosis and ultimate safe prognosis should include, besides the careful clinical history, the microscopic and chemical picture of the urine, the blood pressure study, the cautious physical examination—indeed every detail bearing on the individual case and the modern renal sufficiency tests. However it should be fully understood that the prognosis of the nephropathies (nephritides) is scarcely justified from the determination of the diminution in total renal function alone, for we have learned that the tests do not make absolutely clear the type of nephritis present in the individual case, nor does the fact that

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phenosulphonephthalein is mainly excreted by the tubules justify "the type of the pathological lesion in a case of nephritis" (Christian). The diagnostic and prognostic value of the functional renal tests is further weakened because of the failure of good observers to reach parallel results. The opinions as to the "locus of excretion of the several substances are not in accord" (Christian).

Victor Blum says: "It has been shown that the results obtained by examination of the urine (quantity and chemical examination) are often insufficient to establish the proof of renal competency or incompetency. At the best, these results gave us an idea of the momentary functional condition of the kidney, of its effective work at the time."

"Our modern functional diagnosis, however, has a broader aim. We want not only to learn to recognize the work actually performed by an organ, but must attempt to gain an idea of its maximum capacity for work, its possible extent of function." . . . "When renal impairment exists in company with satisfactory compensation, there will be no symptom whatever of renal incompetence as long as the store of latent reserve force is sufficient to guarantee the excretory function of the kidneys. In the pathology of the kidneys however, particularly in surgical treatment, the important question arises whether the organ will be adapted to increased demands (e. g., in cases where unilateral nephrectomy is intended)." Blum in his enthusiasm says: "The old clinical methods give us no information on this point; we can only designate a kidney as sound in a functional and anatomical sense when we have shown how it carries out the various departments of work forced upon it in experiment."

It may be assumed, further, that at present the results of accumulated experimentation do not establish a positive relation between kidney function and pathological change basing these on the rapidity of excretion of lactose, (Schlayer) potassium iodid, salt and water. Schlayer's pioneer work is based upon large clinical and experimental study. He contends that *vascular nephritis*—acute and chronic—is characterized by retarded lactose excretion, that the oliguria and polyuria depend upon the influences of the vasodilators upon the renal vessels whether the latter are sensitive or insensitive to the former, and the normal excretion of the iodids and chlorids. *Tubular nephritis*, it is held, is characterized by delayed chlorid and iodid excretion, with the water and lactose output normal.

Christian, considering the work of Schlayer and his associates in this field, says: "Still it is undoubtedly true that in functional studies of experimental toxic nephritis anatomical lesions do not parallel closely functional disturbances, and so from these studies it was to be anticipated that in man there would continue to be some discrepancies between clinical diagnosis, even though based on functional tests and demonstrable structural changes in the kidney. These particular functional tests have

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yielded valuable information, but so far they have failed to serve as an adequate basis of diagnosis of type of renal lesion."

He further contends that too few cases examined functionally have been submitted to the subsequent histological examination of the kidneys to justify the complete acceptance of the significance of these tests.

The tests of Schlayer are most valuable in establishing early renal change. They offer but little assistance in differentiating the vascular and tubular varieties of nephritis, and it is generally conceded that because of the diffuse character of the lesion in chronic nephritis, they offer but little of value for diagnosis or prognosis (Piersol).

"The most valuable single aid to the estimation of *total renal function* which is known at present" is that devised by Rowntree and Geraghty which makes it possible to determine the total renal function in all forms of nephritis whether acute or chronic (Fitz). *The phenolsulphonephthalein test of Rowntree and Geraghty* shows the quantity of the dye eliminated through the kidneys within a given time. It has been further demonstrated that the extent and severity of the kidney lesion is in direct proportion to the quantity of phthalein eliminated within that given time.

The test is easily applied and is innocent, causing no local irritation nor constitutional disturbance. The object of the test is to give the clinician an approximate idea of the ability of the kidney to perform its function. Rowntree contends that the "phthalein test is of prognostic value in all pathological conditions, whereas certain cases of severe nephritis, even in uremia, show no marked increase in incoagulable nitrogen or urea." Rowntree, who may be considered the leading authority on this subject, is absolutely fair in his statements, for he insists that "*functional studies reveal only the excretory capacity of the kidney. By themselves they do not make the diagnosis nor settle the prognosis.* Just as routine blood examinations occasionally reveal an unsuspected leukemia, the routine use of functional tests bring latent kidney involvement to light." It is not often that, as in a case reported by Rowntree, functional tests (phthalein) will be required to differentiate and prognosticate diabetes insipidus, but it can be easily understood that such differentiation by the renal sufficiency test may promptly change our conception of the case and lead to accurate prognosis.

To be of value for the prognosis of internal disease the extent of kidney invasion can only be determined by adding to the careful clinical study of the case, the knowledge gained by repeated functional tests (phthalein). The regenerative power of the kidney cannot be ignored; the improvement of the cardiovascular condition and the relief from increased skin and bowel function are factors of great prognostic value, particularly in the *chronic nephropathies*, i. e., interstitial nephritis more particularly. In cases of the chronic nephropathies which show progression, in which the clinical history is usually characteristic and suggestive,

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the progressive lowering of renal function argues in favor of early uremia. With renal obstruction, calculosis—hydronephrosis, abscess—the prognosis is less grave with reduced elimination as demonstrated by the phthalein than with a similar find in the chronic or acute nephropathies.

On general principles it may be concluded that whenever the kidney fails to eliminate phthalein it is proof of renal insufficiency, and the prognosis should be guardedly given—it is usually bad.

In all nephropathies the prognosis based upon the tests can only include a knowledge of the efficiency or inefficiency of the organ. "Death may occur from innumerable other factors concerning which (the tests) they give no information" (Rowntree).

In *acute uremia* the impairment of function is clear without any functional test, though the test gives positive information. In fatal uremia there is practically no trace of the dye, or but little, during the two hours of observation. If in mild cases of nephritis with fair quantity of urinary secretion and nervous manifestations, repeated functional tests show normal or approximately normal output of the phthalein, the prognosis is good and the symptoms are not likely to be of uremic origin.

With nephropathies and symptoms referable to the brain, the eyes, or the gastro-intestinal tract in which uremia is strongly suspected, the sufficiency test will give valuable information, making the diagnosis of uremia or threatening uremia possible in many cases without inconvenience to the patient, while the forecast is consequently strengthened.

Clinical observations by trustworthy observers prove that with both chronic and acute nephropathies the functional tests may occasionally give figures which approach the normal (or they are normal) and yet uremia may promptly follow and may be fatal (Foster-Baetzer). I advise against relying upon functional tests alone in deciding upon the possibility of uremic poisoning in cases in which the clinical, including the urinary (chemical and microscopic) features, are strongly suggestive.

When the nephropathies are associated with *cardiovascular symptoms* (failing heart and renal engorgement) the output of the dye is materially reduced. Under such conditions the increased and timely excretion of phthalein is encouraging and indicates improvement of the heart, relief of congestion and, for the time at least, danger reduced. When the heart symptoms improve and the functional test shows lowered excretory capacity persistent, the nephritis is grave and the prognosis correspondingly bad.

The tests for the estimation of the incoagulable or nonprotein nitrogen of the blood are valuable, but are complex and cannot easily be used by the busy clinician without a well-trained laboratory assistant. The study of the retention of urea in the blood is of great prognostic value. The range easily computed by the Armard formula establishes 1.0 as the standard. High readings are found with advanced chronic nephritis and run parallel with increase of symptoms (See References for method, etc.).

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These studies are of great prognostic value for they prove "the stage of accumulation of waste products, an accumulation that may vary from almost normal figures to enormous increase in uremia" (Elliott).

The experimental observations of Frothingham, Fitz, Folin and Denis with uranium nephritis show that the non-protein index in the blood and the phthalein test run parallel as "indicators of renal function, varying from normal during the course of the nephritis and returning to normal as the nephritis heals" (Elliott). These observers hold that while the phenolsulphonephthalein excreted offers the index of the kidney function at the time tested, study of the non-protein nitrogen content of the blood shows the accumulated difference between manufactured effete or waste nitrogen bodies in metabolism and the quantity actually excreted.

Cumulative symptoms follow, when excretion of the dye (phthalein) falls below 40 per cent in two hours (Agnew, Folin, Otto and Seymour). The reader is referred to Mosenthal's article for the consideration of the prognostic value of renal function as measured by the estimation of fluids, salt and nitrogen, and the specific gravity of the urine; also Janeway's recent paper (See References).

Another important prognostic feature has been noted by Rowntree, Fitz and Geraghty in chronic secondary congestion of the kidney, in which the secretion of the phthalein in the urine is reduced, but the incoagulable nitrogen of the blood is not materially increased. Agnew has thus succeeded in differentiating the cardiac from cases in which the kidney invasion is in the ascendency; Foster suggests that this holds for the milder circulatory obstruction but with graver circulatory lesions in which there is non-protein nitrogen excess, the criterion is not dependable.

It seems to the author that the confirmatory evidences of anatomic lesions by Thayer and Snowden are among the strongest evidences of the value of the phenolsulphonephthalein test in prognosis. These observers compared the lesions found on autopsy with the previously made tests in 54 cases of nephritis of varying types. In all cases of grave nephritis they found a decided reduction of excretion of the dye. They contend that their experience proves a progressive lowering in the excretion of the dye, and this they have learned to consider of considerable value in prognosis. They make the strong statement that during a period of five years they have never met with a severe case of chronic nephritis in which there was a satisfactory excretion of phenolsulphonephthalein.

The observations of Thayer and Snowden were confirmatory of the conclusions offered by Rowntree and Fitz, that with chronic kidney congestion and reduced dye excretion the normal may be reached as the heart compensation is established. The tolerance which is often established by the individual to uremic and toxic states becomes an important factor in prognosis, and under such conditions it will be found that the dye excretion may remain abnormally and surprisingly low during long periods;

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on the other hand, as has been demonstrated by Arnold, proper living (rational diet) in these cases often holds patients with marked renal insufficiency during months and years.

The results of renal sufficiency tests are often contradictory. Serious clinical manifestations are often at variance with the functional test, and vice versa, mild clinical evidences of nephritis are associated with surprisingly low values. Elliott expresses the opinion of the advanced clinician. He says: "In view of the long recognized fact that it is impossible to predict accurately by clinical study alone what course the disease will take in development, it would appear that we should at least accept the results of function study as a qualifying factor in prognosis."

The early application of the sufficiency tests was largely limited to surgical cases by Rowntree and Geraghty. The most recent article dealing with the surgical aspect of this question is from the pen of Braasch and Thomas, of the Mayo Clinic. The material of these observers is large and has been carefully tabulated. It is not within the province of this work to consider the prognostic value of the tests from the surgical point of view, but it may be assumed that the authors mentioned are correct when they hold that "probably the greatest value of the functional tests will be as an aid to the diagnosis of doubtful lesions of the kidney."

The urologist has given us valuable diagnostic and prognostic data in obscure cases from ureteral catheterization and associated renal sufficiency tests of the separate kidneys. It can be easily understood that in cases where surgical interference is indicated such study may prove invaluable for prognosis and therapy. Braasch and Thomas in their concluding paragraph say, after acknowledging the scientific efforts of Rowntree and Geraghty: "The phenolsulphonephthalein test, because of the ease of application and rapidity of secretion, remains as probably the best functional test at our command. Nor is it our purpose to detract from the value of a careful examination of the character of ureteral secretion in surgical conditions of the upper urinary tract. It is our contention, however, that the fundamental surgical principle and clinical data should determine whether or not an operation is indicated; and that renal functional tests are of practical value, largely as an aid to differential diagnosis and only to a limited degree as a prognostic aid." Clinicians are inclined to subscribe to the dictum of Christian as safe, in the light of our present knowledge and experience.

"As in all forms of clinical diagnosis, not the single test, but many, yield the data on which diagnosis must be based. In this sense these functional tests have yielded new data, and a discriminating evaluation of this new data along with a consideration of data furnished by other methods of examining our patients already long in use, justify us in making diagnosis of renal condition with an increased certainty. We can expect fewer failures in renal diagnosis than before we had these

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functional tests, but so long as microscopic study fails to yield a demonstrable anatomical change to correspond with all observed functional variations, so long will we remain unable to make in advance an exact anatomical diagnosis which in most cases will prove to be correct when the pathologist examines the kidneys."

Urinary cryoscopy—the determination of the freezing point by means of the Beckmann thermometer, an exceedingly delicate instrument—has not been accepted by the profession as a means of much value in determining the total renal efficiency.

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(*f*) *Bacilluria—Bacteriuria*

When the urine is laden with disease-producing germs, the condition is known as *bacteriuria* or *bacilluria.*

Most cases of bacilluria are symptomatic—secondary to general infection due to the Bacillus typhosus, the Bacillus coli commune, streptococcus or gonococcus—or they arise from foci either in the bladder or somewhere within the genito-urinary tract. It is often exceedingly difficult, in fact impossible, to decide whether the bacilluria is due to the entrance of

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germs (as in typhoid fever) directly from the blood stream to proliferate in the kidney or urinary passages or whether there may not be a focus somewhere within the urinary passages, often giving rise to no symptoms, which surcharges the urine. When bacilluria is due to genito-urinary infection (local) the prognosis is almost always good and depends entirely upon the nature of the primary disease.

With the bacteriuria of constitutional infection there is rarely a local lesion in the kidney. With the grave infections, or even some milder infections, there may be but slight evidence of bacilluria though nephritis often complicates the primary disease and materially influences the outcome.

Pyuria (*purulent urine*) is an indication of bacteriuria. The prognosis depends on the ability to reach the focus responsible for the secondary infection. *Moderate and transitory bacteriuria may be normal* and insignificant, for in over 50 per cent of normal individuals the urethra holds bacteria (Kelly and Burnham). (See also Lustgarten & Mannaberg, Rovsing, Savor, Hofmeister and Chvostek.)

Cystitis is the cause of a large number of bacillurias. This is a surgical field, which offers an excellent prognosis when rationally treated. The reader is referred to the article of T. R. Brown dealing with the bacteriuria of cystic origin.

As a rule, the fresh urine of normal subjects does not show bacterial contamination. With true bacteriuria it is exceedingly difficult, even in the fresh specimen to overcome the turbidity of the urine entirely.

Bacteriuria or bacilluria is frequent with *diabetes mellitus, tuberculosis of the genito-urinary tract, purulent kidney, embolic nephritis, scarlatinal nephritis and infectious jaundice* (Weil's disease).

Spaeth includes among the pathologic bacteria causing bacteriuria:

1. *Bacillus Tuberculosis.*—Every purulent urine which persists, should be suspected to be of tuberculous origin; only repeated examinations will clear the diagnostic and prognostic horizon (See Tuberculosis of the Kidney).

2. *Gonococcus* (See Gonococcemia).

3. *Bacterium Coli Commune.*—This bacilluria is likely to be resistant at times; the urine is persistently acid.

4. *Typhoid Bacillus.*—The typhoid bacillus in the urine demands cautious attention; it is of greater danger to those who surround the carrier than to the host.

5. *Staphylococcus*
   (a) Staphylococcus pyogenes aureus
   (b) Streptococcus pyogenes

6. *Streptococcus Pyogenes Ureae*—The urine is alkaline as a rule. The process is usually rebellious.

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7. *Streptococcus with Acute Nephritis* (See Acute Nephritis)
8. *Streptococcus Cystitidis*
9. *Bacillus Septicus Vesicae*
10. *Bacterium proteus fluorescens*
11. *Proteus vulgaris Hauser.*

The *actinomycotic or the ray fungus,* the *saccharomyces* (particularly with diabetes), the *mycelium,* the *Penicillium glaucum* and with pregnant women the *Oiduim albicans,* may cloud the urine.

Most bacillurias offer a favorable prognosis; all demand the thorough consideration of the primary condition before any forecast is justified.

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(g) *Chyluria*

(a) Chyluria
(b) Lipuria

Prout named the condition "chylous urine," a disease mainly of tropical climates.

(a) Chyluria

Chyluria is never normal—fat is not a normal ingredient of the urine. Chyluria may be either *parasitic* or *non-parasitic.*

Parasitic chyluria is found in the tropics; the urine is characteristic for it contains the constituents of the chyle, fat, lymph cells, blood corpuscles and soluble albumin. In some urines cholesterin and lecithin are present. In the milder cases the urine may be bloody and decomposes easily.

The chyluria due to the *Filaria sanguinis hominis* is not directly dangerous, per se; it is chronic; causes considerable drain and weakness, often persistent anemia; it limits the activities of the patient and makes him wretched.

In pregnant women the symptom when infected is markedly aggravated, probably because of the rupture of a lymphatic varix into the bladder (See also Filaria Sanguinis Hominis).

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(b) LIPURIA

(See also Lipuria in this Section, Subdivision b).

Lipuria is not a true chyluria. With fatty degeneration of the kidney and marked parenchymatous breakdown and milky urine, lipuria may occasionally occur; the same condition may be associated with or follow phosphorous poisoning; it is also found in pregnant women. With kidney complications—*chronic nephritis or acute nephritis*—there may be abundant sediment on centrifuging including degenerated epithelia and casts.

With *obstruction of the thoracic duct* due to the pressure of nodules, adhesions or large-sized growths, chyluria may be a symptom of the primary disease. In all forms of *non-parasitic chyluria* (not lipuria) the chyle must in some way gain entrance to the urine through a leaking chyle-carrying vessel. It happens occasionally after *fractures* that fat gains entrance to the urine and causes lipuria (See Lipuria).

Contusion or compression of the liver or fatty growths may cause fatty urine. Lipuria may be a symptom of diabetes mellitus, tuberculosis or obesity. There is danger of fat emboli in some of these cases; fortunately the complication is rare. Prognosis of uncomplicated lipuria depends upon its cause (See Lipuria).

Non-parasitic chyluria may persist during many years; there may be latent periods long or short followed by exacerbations, until finally the symptom may disappear never to return. The attacks may last during varying periods—few weeks, months or years. Normal urine is voided during remissions (See also Filaria Sanguinis Hominis).

The majority of non-parasitic chylurias offer a favorable prognosis; though obstinately chronic, life is not often threatened.

(*h*) *Phosphaturia*

The deposition of the phosphatic content of the urine depends upon its reaction. The earthy phosphate of lime and magnesia are soluble in the acid urine; neutral and basic phosphates of lime and magnesium show strong tendency to be deposited in urine which is but slightly acid, neutral or alkaline. The phosphates are derived principally from the food but also from the tissues. Brain workers, nervous individuals, tuberculous subjects, patients with marked wasting, with the grave anemias and degenerative atrophic diseases of the liver show increased production of phosphoric acid.

During pregnancy and with many acute diseases the loss of phosphates is reduced early, to increase with the advance of the infection. Normally the urine is alkaline after meals and the phosphates are apparently increased. The diminished acidity of the urine, or alkalinity, often

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causes a turbid urine to be voided after eating—which is by no means to be interpreted as pathologic or significant. Only the quantitative estimation of the phosphates is of value for diagnostic or prognostic purposes.

If the clinician wishes to reach conclusions he must estimate the loss of the earthy and triple phosphates, rather than depend upon the total amount of phosphates eliminated through the urine, and this during twenty-four hours. With *ammoniacal fermentation* of the urine there is a precipitation of amorphous phosphates without indicating an abnormal loss of phosphoric acid, hence not a true phosphaturia. In treating certain urinary conditions (uric-acidemia, calculosis, etc.), Roberts years ago called attention to the advantage of keeping the urine alkaline during the greater part of the day by eating small quantities at short intervals. In these cases the changed reaction shows marked phosphatic deposit, which means nothing prognostically.

In nervous patients with marked neurasthenia, with diseases characterized by polyuria (diabetes insipidus, diabetes mellitus, diseases of the sexual organs) the voiding of a clouded alkaline or weak acid urine causing the "phosphate cloud" often leads to great fear on the part of the patient. Autosuggestion may follow, and it is with the greatest difficulty that the clinician is able to impress the patient with the insignificance of the symptom. To the average patient's mind, the clear urine is without danger, but the clouded or milky urine in which there is only a changed reaction to cause the deposit, as a rule, is associated with the gravest possible genito-urinary diseases.

With a *decrease of intestinal excretion in children*, particularly with some forms of *colitis*, there is often an increase in the calcium phosphate in the urine. The prognosis of true phosphaturia dependent upon faulty diet, or functional disturbances, is positively favorable. With brain workers, the neurasthenic and hysterical patients who are physically and mentally fatigued, the element of rest is important and when fully appreciated and acted upon improvement of all symptoms is the rule. When in the neurotic it is found that calcium metabolism is at fault and that as a result there is an abnormally large calcium phosphate loss, diet, rest and rational treatment continued during a sufficiently long period, will lead to general improvement as well as normal metabolism.

The presence of triple phosphates in the urine (ammonio-magnesium phosphates) is, as a rule, dependent upon bladder infection or organic disease of that organ. It is only one of the conditions to be considered in offering the forecast—the primary disease alone makes prognosis possible.

The normal amount of phosphoric acid excreted daily is from 1 to 5 grams; the amount of earthy phosphates from 2 to 2.5 grams.

Cases of so-called "phosphoric diabetes" or "essential phosphaturia" have been reported (Teissier) and are occasionally met in practice (rare —but one in 6,500 cases of internal disease seen by the author) in which

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the condition is chronic. There are many symptoms of diabetes, including polyuria, great thirst, progressive emaciation and enormous loss of phosphates, in some cases as high as 8 to 10 grams daily. These patients may die with symptoms of acidosis, just as diabetics die in spite of the fact that the carbohydrate output has been found normal with a high organic phosphorous percentage. According to Barker the leading feature in a case which he studied was an abnormally large amount of organic acids.

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(*i*) *Oxaluria*

Oxaluria *per se* has never in my practice threatened life, nor has it often required consideration except as the precipitation of calcium oxalate in the kidney or bladder, which because of its insolubility has led to the formation of calculi.

The daily output of lime oxalate is largely dependent upon the food ingested, though a small amount is excreted on an absolutely oxalate free diet. Hence it may be safely assumed that the normal small oxalic acid output (1 to 2 mg.) daily is of exogenous origin (vegetable foods mainly) and the remainder is endogenous. The entire oxalic acid output daily in the normal urine is 10 milligrams. This is held in solution in the form of a salt by the acid phosphate of sodium normally present in the urine.

The "*oxalic acid diathesis*" was introduced when Donne (1838) demonstrated lime oxalate crystals in the urine. In practice we frequently find acid dyspepsia associated with oxaluria. Garrod says: "The administration of hydrochloric acid has been shown to promote the absorption of calcium oxalate from the food and to increase the urinary output; and it is probable that in the cases described by Begbie and others as examples of an oxalic acid diathesis attended with neurasthenic symptoms, the deposition of oxalate crystals in the urine was, as Dunlop suggested, largely due to such increased absorption as the result of the acid dyspepsia which was a prominent phenomenon of the condition."

Proper diet and the regulation of conditions which will best hold the oxalates in solution make prognosis favorable. The presence of free hydrochloric acid in the stomach contents and its administration when absent, besides the prevention of intestinal fermentation will do much to prevent oxaluria in individual cases. In some, there is no known

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explanation of the tendency, and unless calculosis follows, these patients are fairly comfortable as a rule. These conditions are usually transitory, though in some subjects there is a marked tendency to the precipitation of lime oxalate. The calculi formed are hard and irritating, easily recognized by x-ray examination and usually amenable to surgical treatment.

Crofton probably expresses the truth when he says: "The clinical significance of oxaluria in the light of our present knowledge is slight. When oxaluria is not alimentary, it presumably indicates some oxidative perversion, leading to incomplete metabolism of uric acid and of blood sugar, occasionally it may indicate derangement of the liver function."

In *diabetes* and in *icterus*, oxalic acid in large quantities is found in the urine in some cases.

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(*j*) *Indicanuria*

Indican—i. e., *indoxyl sulphate of potassium*—may be present in normal urine in small, but easily recognizable quantities. It is but one product of intestinal putrefaction; putrefaction may go on in the intestinal tract without indicanuria.

E. E. Smith has called attention to marked gastrointestinal toxemia without excessive indol absorption. Brunon and Gibert have proved that the proportion of the ethereal sulphates to the total nitrogen of the urine is a nearly constant one in health, which rarely falls below 1 to 100 and never rises above 1.40 to 100.

Indol which is resorbed from the intestinal canal is oxidized in the tissues of the body to indoxyl and is converted into indoxyl potassium sulphate in the urine where it is bound to potassium sulphate. The formation of indol in the intestinal tract depends upon bacterial action. The albumin content is decomposed in the presence of the bacteria.

Indicanuria *per se* is not of great prognostic significance; it is often symptomatic of functional or organic disease and may in occasional cases prove of diagnostic importance. This is true of cases in which there are but scant or unsatisfactory symptoms of intestinal obstruction, also with peritonitis, Asiatic cholera, malignant and ulcerative diseases of the stomach and intestines. The depth of color with intestinal obstruction is of some prognostic and diagnostic value; considered alone it is valueless.

Indicanuria—associated with *gastro-intestinal indigestion* and the evidences of *auto-intoxication indicanuria*—is not the principal disease, simply a symptom and as such it should be interpreted (Forchheimer).

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Of 77 cases examined by Forchheimer, 68 showed indicanuria. The formation of intestinal toxins which are responsible for indicanuria takes place in the lower segment of the small intestine and in the colon. Morgan holds that the chief distributing center is the colon, and he asserts that "imperfect digestion of proteid foodstuffs in the small intestine is the leading cause." He further holds that "depressed nerve action due to overwork or disease, amounts rather than quality of food taken in excess of the ability of the intestines promptly to take proper care of it, too great preponderance of one class of food taken over too long a period when at the same time there may be more or less nerve depression" are among the most frequent causes of disturbed intestinal digestion which are responsible for indicanuria.

There are indicanurias not easily influenced by treatment in which it is often exceedingly difficult to define a cause and in which, barring symptoms (usually insignificant, never threatening early) the condition persists during many years. These cases are characterized as *"chronic intestinal toxemia"* and are unquestionably responsible with other toxic products for distant changes in heart, arteries and kidneys in a large number of cases.

Lesions of the intestinal mucosa, however slight, continue indicanuria during unlimited periods. The greater the epithelial change the more persistent is the indicanuria. Normal epithelium offers a barrier to the formation of indol and its resorption from the intestinal tract (Herter and Wakeman).

Constipation *per se* is not a cause of indicanuria (Jones, Houghton); Forchheimer's experience does not agree with Jones' conclusion. The former found indican in 39 of 44 cases of constipation. Baar in his recently published work enters minutely into all the possible factors which cause indicanuria. For purposes of prognosis I have considered the literature included by Baar and the diseases of which indicanuria may be a symptom. 2,037 patients were examined and 8,406 tests for indican were made of which 4,039 were positive and 4,007 negative.

There are but few diseases in which repeated examinations of the urine for indican will fail to give positive results at some time during their course.

It is safe to conclude that the majority of indicanurias *per se* are of minor significance; that with chronic intestinal diseases, indicanuria is a prominent symptom and indicates intestinal putrefaction; that many grave diseases, cancer and ulcer of the intestine, large and small (particularly if causing obstruction), are associated with marked indicanuria; that indicanuria is often an expression of a chronic toxemia in which there are also other toxic substances which when neglected may after long periods invite distant degenerative changes in vital organs (heart, arteries and kidney).

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Bacterial action is required to produce putrefactive fermentation in connection with the production of indican (Senator, Porter).

The toxins formed at the same time as indol are absorbed into the circulation from the alimentary canal and by their combined action cause a train of nervous symptoms.

Conditions which favor the production of indican are improper diet, lack of exercise, mental strain and fatigue, perverted gastro-intestinal secretions and abnormal gastric and intestinal mucosae.

In my last 6,540 cases of internal disease 50 per cent showed either a trace or considerable indicanuria some time during observation.

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(*k*) *Urobilinuria*

The clinical significance of urobilin in the urine is often of considerable importance. Meyer-Betz in his most exhaustive study of the subject holds that urobilin is produced from bilirubin, and he accepts the conclusion of Friedrich Mueller that the transformation takes place in the intestinal tract (enterogenous, in contradistinction to the hepatogenous theory). Without bile in the intestine urobilinuria is impossible. *Urobilinogen is the antecedent of urobilin and the two cannot be divorced.* Urobilinogen is often present in normal urine in very small quantities, and gives the urobilin reaction only when exposed to air and light or by the action of acids (Wood).

Whenever urobilin is present it may be concluded that the liver parenchyma has suffered, that bile is finding its way into the intestinal tract. If the intestinal tract were absolutely free of bacterial contamination, with bile in the intestine there would be no urobilinuria. In the newborn there is no urobilinuria; after the third or fourth day it may appear with the appearance of germ life.

With stricture of the common duct sufficient to prevent the onward flow of bile, however grave the disease, urobilinuria does not appear.

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Small quantities of urobilin in the urine are of no prognostic significance; large quantities are evidence of disease, except during the last days of pregnancy when its presence may be considered to be normal. For diagnostic and prognostic purposes it should be remembered that it is impossible to consider urobilin separate from urobilinogen, for the transition of urobilinogen as already suggested to urobilin is usually prompt and rarely fails to take place.

Urobilinuria is frequent with *scarlet fever* (Jugendreich) particularly with the malignant or more severe types. The mild cases of *measles* may show moderate urobilinuria, the more severe are likely to give positive reaction. The fact that urobilinuria has been demonstrated with German measles would prove that for the prognosis of the exanthemata it is unwise to consider its presence of great value.

Urobilin may be present in the urine of *typhoid patients* during the active periods of the disease and is often found during convalescence. It is not expressive of the severity of the infection; it is, however, influenced by the extent of intestinal lesions and resulting diarrhea.

With *bacillary dysentery* urobilin is absent from the urine; with the amebic variety it is only found when there are liver complications, i. e., abscess (Justi).

Urobilinuria with *acute polyarthritis* is always indicative of severe infection. Hildebrandt found it in 50 per cent of all cases.

With *septicemia* urobilinuria is only present when there are liver or heart complications; with *erysipelas* it is usually present early and persists until convalescence has ended; the same is true of *meningococcus erysipelas.* With *pneumonia* urobilinuria is usual. When jaundice is present the prognosis is serious—otherwise it is not of moment. With *pernicious malaria* urobilinuria is present and reduces the effect of quinin (Simpson and Edie). The severe types of *yellow fever* and *relapsing fever* are rarely without urobilinuria.

Urobilinuria with *pulmonary tuberculosis* is rarely present in mild or incipient cases; it is an accompaniment of advanced tuberculous, general infection. Hoppe-Seyler found but slight urobilinuria with acute miliary tuberculosis, and that urobilinuria followed the injection of tuberculin.

With *heart lesions* it may be concluded that well compensated faults are without urobilinuria; that with an extra tax upon the heart, with broken compensation, it promptly appears to disappear with improvement in heart tone. With evidences of stasis (renal and hepatic) urobilinuria is to be expected. This is the more evident when organic disease of the liver coexists, and Jonas has demonstrated the greater frequency of urobilinuria with disease or failure of the right heart.

Urobilinuria is not prominent with the *nephritides or nephropathies* unless there is associated infection or organic disease of the liver. With *infectious pyelitis* during pregnancy I have found urobilin in the urine.

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The case terminated favorably for mother and child and the grave anemia which was threatening yielded promptly.

Ulcer of the stomach and cancer, when uncomplicated, are without urobilinuria. When there are *metastases,* or with added *infections,* the condition is reversed (Infectious gastritis) (Meyer-Betz).

The presence or absence of urobilin from the urine with other *intestinal diseases, including peritonitis, appendicitis, obstinate constipation,* is of no prognostic value.

With alcoholics persistent urobilinuria is at least suggestive of advancing liver change. With acute alcohol poisoning urobilinuria is prominent. *Discontinuance of alcohol, unless there are deep liver changes, is followed by disappearance of urobilin from the urine.*

Poisons, such as carbon monoxid, chloroform, antifebrin (Friedrich Mueller) sulphonal, trional and salvarsan may cause liver changes leading to urobilinuria.

Urobilinuria with the *diseases of the blood* may be present; rarely with uncomplicated *chlorosis;* often with *pernicious anemia* and *bothriocephalus anemia.* The *leukemias* in the terminal stages and with *acute leukemia* often show urobilinuria, as do *Hodgkin's disease* and *purpura.*

Almost all *diseases of the liver* in which the bile finds its way into the intestinal tract are associated with urobilinuria. The most prominent of these is *Laennec's cirrhosis.* In this disease urobilinuria may precede other evidences of organic change. Meyer-Betz calls attention to the frequency of urobilin in the blood and ascitic fluid of these patients.

Hypertrophic cirrhosis and *Banti's disease* are almost always found with urobilinuria. I have, in connection with other grave diseases of the liver hemolytic jaundice and the degenerative diseases of the liver, called attention to urobilinuria as a symptom and have considered its prognostic significance (See Diseases of the Liver). It may be safely assumed that the more severe and deep the changes in the liver parenchyma, the more marked is the urobilinuria. *The presence of urobilinuria will often prove of great value in deciding upon the functional ability of the liver; it should never, however, be given precedence over subjective symptoms or objective signs.* Large cancer masses in the liver are usually found with urobilinuria, not so with small nodules always. It is safe to conclude that infectious processes when associated with urobilinuria are complicated with liver degeneration. Whatever the disease of the liver, if the common duct is occluded, urobilinuria is invariably absent.

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(*l*) *Other Substances*

Among the leading urinary anomalies which have not been considered in the preceding pages are:

Lithuria
Cystinuria
Melanuria
Alkaptonuria
Pneumaturia
Lipuria
Lipaciduria
Hematoporphyrinuria

Lithuria

Lithuria and the uric acid diathesis are considered in connection with the study of the prognosis of gout and the consideration of urinary changes with many functional and organic diseases.

Free uric acid is insoluble and is found only in hyperacid urine.

Uric acid is held in normal urine in solution and as the ammonium, sodium and potassium salts, i. e., urates. When uric acid is precipitated it is present in increased and abnormally large quantity, the acidity is high, the mineral acid content is low as is also the pigment. The prognostic significance of uric acid in the urine has been enormously exaggerated; excessive production and faulty elimination cause symptoms to which the proper significance has been given in the *Section on Metabolic Faults.*

The precipitation of the *amorphous urates* causing the "brick dust deposit" (acid sodium urate) from the cool urine is of no great clinical or prognostic significance. Often the urine is excessively acid and concentrated (specific gravity high). The underlying conditions, if there are any which are abnormal, offer their own prognosis.

Cystinuria

Usually cystin when found in the urine is indicative of calculosis either of the bladder or kidney pelvis. I have seen but few cases of

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cystinuria in which there were no symptoms of stone. One of my cases of cystinuria, seen over twenty-five years ago, has never so far as I have been able to determine from x-ray or bladder search, formed a calculus, and has not been affected by the persistence of the symptom. Most cystinurias are congenital and hereditary. My case showed no hereditary predisposition. In the case of a babe, aged twelve months, I removed, over 25 years ago, a cystin stone which was caught in the urethra; there never was return of cystinuria. Now grown to manhood, there are no evidences of anything abnormal in the urogenital system.

Melanuria

Melanuria or "black urine" may be due to one of several causes.

True melanuria (melanin, phymatorhusin) is due to the presence of a pigment of unknown origin which is, in all probability, derived from blood pigment. It is not *per se* of prognostic value, but occurs with a grave condition (melanosis) in which there are multiple melanotic or sarcomatous growths. With marasmus and reduced (cachectic) patients melanuria may persist without melanotic growths. It is not pathognomonic of melanotic cancer and is not always present with such growths, though it may be.

With *deep jaundice* the bile salts and coloring matter are responsible for the "black urine." Jaundice with black urine is usually grave, often of malignant origin.

It is exceedingly rare to find benign indicanuria so deep as to cause black urine; the malignant intestinal obstructions may occasionally offer black urines due to excessive indicanuria. During the early days of antiseptic surgery when the spray was used and open surfaces were long exposed, black urine with other evidences of carbolic acid poisoning was frequent. Such complications added an element of danger because of interference with renal function. The long and injudicious use of salol, salicylates, carbolic acid, resorcin and some coal tar preparations may be followed by black urine. The associated symptoms and general condition of the patient with the primary disease make prognosis easy.

Alkaptonuria

I have never in practice met a case of alkaptonuria. It is an exceedingly rare condition, usually found in males; it is always congenital and persists during life without interfering in any way with the general condition or activities of the subject. There are a number of recorded cases in which several members of a family had alkaptonuria, some in which father and son showed it and in some consanguineous marriages seems to have been a factor.

When alkaptonic urine is first voided it may appear normal, it promptly becomes brown and later black.

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Pneumaturia

Gas in the urine without trauma or mechanical insult is exceedingly rare unless there have been ulcerative changes, such as cancer or pressure (vesicovaginal fistula, vesico-enteric fistula), or as the result of the growth of fungi or germ life (air producing bacillus, colon bacillus), or where, through instruments, air enters the bladder. I recently had a case of cancer of the bladder and prostate with pneumaturia in which no perforation was found; neither was the Bacillus aerogenes capsulatus present. The prognosis of pneumaturia depends entirely upon the primary cause. The condition is usually surgical.

Lipuria

The prognosis of lipuria (fat in the urine) when due to degenerative changes in the kidney parenchyma, fat embolism (usually after fractures), acute or subacute phosphorous poisoning, is always grave. These conditions are not true chylurias.

When the excessive use of fat leads to lipuria it is of no prognostic significance.

In one of my cases a tuberculous pyonephrosis was associated with fat in the urine. Ebstein reports pyonephrosis with lipuria.

I have also seen lipuria with cases of amyloid disease in tuberculous subjects and with long continued suppuration.

Lipaciduria

von Jaksch and Rokitansky called attention to the presence of volatile fatty acids in the urine, including formic, acetic, butyric and propionic acids. Volatile acids in the urine have been found with grave febrile disturbances, profound involvement of the liver parenchyma and the severe type of diabetes mellitus. Lipaciduria when considered alone is of no prognostic value. von Jaksch says that the origin and course of lipaciduria follows the same laws which govern febrile acetonuria.

Hematoporphyrinuria

Hematoporphyrin is hematin without the iron element. Normal urine, according to Crofton, always "contains minimal quantities of this pigment." When hematoporphyrinuria is excessive it is formed in the blood.

Acute sulphonal, trional and tetronal poisoning shows excessively large quantities of the pigment. In Tyson's case of sulphonal poisoning large quantities of hematoporphyrin were passed on three successive days (1.683, 1.013 and 0.098 grams). The author calculated that fully "one-seventeenth of the body hemoglobin was destroyed and wasted in the urine."

The leading grave diseases in which hematoporphyrin may be in-

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creased are diseases of the ductless glands and the blood-producing organs. These include Addison's disease, Graves' disease, the primary anemias, pulmonary tuberculosis, acute polyarthritis, lead poisoning, and Osler mentions intestinal hemorrhages and pleuritic effusion.

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Diseases of the Renal System

The Nephropathies

(*a*) *Acute Parenchymatous Nephritis*

(Acute Tubal Nephritis, Acute Bright's Disease, Acute Croupous Nephritis, Acute Catarrhal Nephritis, Acute Desquamative Nephritis, Acute Nephropathy, Acute Diffuse Nephropathy, Acute Glomerular Nephropathy)

Origin.—Most kidney lesions which are characterized as nephritis are degenerative in the main and are of secondary origin (nephropathies). They are dependent upon toxic substances as a rule, brought to the kidney through the blood stream (hematogenous). These forms of nephropathies have been considered in connection with *sepsis, scarlatina, diphtheria, pneumonia, tuberculosis, erysipelas, Asiatic cholera, typhoid* and *typhus fevers, streptococcus tonsillitis* and many of the other acute and chronic infections.

Determining Factors.—The complication (acute nephropathy of infectious character) with these diseases should never be lightly regarded, and I have with each considered the influence upon the forecast (See Infections, Section I). The resistance of the patient and the virulence of the infection, the depth of the toxemia resulting, are leading determining factors for prognosis.

It is surprising to note that with some epidemics the toxemia is malignant and overpowering, the nephropathy rapidly degenerative, the urinary secretion promptly reduced, the albumin loss in the concentrated urine large, the evidences of degeneration, at times inflammatory changes strik-

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ing, with abundant casts and epithelial desquamation, the uremic symptoms prompt—all favoring an unfavorable termination. In spite of the presence of all of these unfavorable conditions and symptoms recovery is not impossible. There are, on the other hand, infections and epidemics in which there are but few evidences of degenerative changes, moderate albuminuria without marked change in renal sufficiency, no overpowering toxic symptoms, little influence on the cardiovascular condition, in which the prognosis of the primary infection is but slightly modified by the presence of the kidney complication. Mild infections may be complicated by alarmingly severe nephritis while it often happens that the graver infections may escape the complication and an insignificant albuminuria remains the only evidence of renal invasion. This is often true of scarlet fever.

As a rule, the more malignant the primary infection the more likely is nephritis to develop and the more severe does it prove to be. As already suggested this is not always the case. While acute nephritis may be diffuse and the degenerative changes extensive, including vascular changes and abundant exudation, *the disease is, as a rule, glomerular.* With the malignant infections there is a strong tendency to grave degenerative changes, *hemorrhage* and *exudation.* This type of acute nephropathy is always serious, it may complicate diphtheria or other overpowering infections with *scanty urine, abundant casts* (*epithelial, granular, blood* and *hyaline*), *a profound primary toxemia, added uremia, great unrest and myocardial weakness* (rapid pulse).

The Glomerular Type.—The glomerular type of acute nephritis which develops in young adults most frequently (less frequent after middle life, though not uncommon), is found in the male oftener than in the female (3-1), is usually a disease of the middle and lower classes, may develop after *exposure to cold,* after *overheating,* or the *acute infections,* after the *rapid and sudden destruction of the skin* (*wounds and extensive burns*), with *syphilis;* occasionally it proves to be an acute exacerbation of chronic nephritis; it is found with pregnancy, alcohol poisoning, Spanish fly (cantharides), turpentine, copaiba, phosphorus, salicylic acid, arsenic, antimony, potassium chlorate and other drugs.

The Acute Non-suppurative Nephritis of Councilman

This form of nephritis may be associated with acute infection. In these cases there is often a profound toxemia—particularly with the deeper and malignant infections—in which the lymphoid elements are numerous in the renal cortex. There are evidences of involvement of the spleen and bone marrow from which the cells, which correspond with the Unna "plasma cells," are carried to the kidney by the blood. Councilman holds that acute interstitial nephropathy "is the most common lesion of the kidney in the acute infectious diseases of children, particularly

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scarlet fever and measles, less common in uncomplicated cases of diphtheria and in smallpox.

This condition is rare in adults. The lesions most prominent are the "infiltration of the interstitial tissue with large mononuclear cells of an indefinite type often closely resembling or identical with the plasma cells, often closely resembling myelocytes." The cortex and pyramids are also infiltrated; in the renal capillaries and veins these cells are found and the larger mononuclear cells are "actively ameboid." With the more severe cases similar changes were found in the heart muscle, spleen, lymph nodes and other organs of the body. In these cases *the prognosis must always be considered grave because the cell accumulation is dependent upon anomalies of the blood primarily.*

Nephritis Complicating Infections.—Careful consideration of the histories of the acute nephropathies establishes the fact that almost all are preceded by an acute infection. Many acute infections which lead to nephritis are so mild as to receive but little attention. *No acute infection, however mild or limited,* is *without the possibility of complicating nephritis. Many chronic nephropathies originate in neglected and undiscovered acute nephritides.*

Acute syphilitic nephritis has been separately considered (See Syphilis of the Kidney). It usually arises in the secondary stage and within the first year. My cases have usually yielded to treatment. *In some of these, edema, dropsies of the serous cavities and urinary conditions have seemed threatening and unfavorable, but recovery though slow, is usually complete.* One of my acute specific cases was water-logged and uremic, and demanded repeated paracentesis abdominis, yet he made a full recovery without leaving a remnant of kidney disease discoverable by repeated tests and long surveillance.

Outlook.—In *grave cases of acute nephritis and primary infection* the development of the former complication may cause *sudden serious cardiac weakness* after a distinct chill and almost complete anuria with or without evidences of uremia. *Increase of the constitutional symptoms,* particularly the nervous manifestations of the primary disease with acute nephritis, always demands the closest consideration, for the sudden abeyance of kidney function in such cases, continued twenty-four to forty-eight hours, is among the leading dangers.

Cases in which the added kidney infection is without marked influence on the subjective or objective features of the primary disease, in which the quantity of urine is not markedly decreased, without dropsy of the serous cavities, though edema may be present, without uremia, offer a good prognosis.

Acute nephritics who develop uremia early with convulsions, who fail to respond to treatment promptly, in whom the circulatory symptoms are prominent, with early changes in blood pressure, with or without persist-

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ent vomiting, offer a doubtful prognosis. The early invasion of the heart (hypertrophy) and vascular (arterial) changes, with bounding pulse and relatively high blood pressure, and high pulse pressure, are always evidences of far-reaching kidney invasion.

Marked reduction in the quantity of the urine, large albumin loss, abundant evidences of desquamation in the presence of renal epithelial cells, casts and blood corpuscles with uremic symptoms always demand the most guarded prognosis.

Bloody urine is not always of prognostic significance. Some cases, scarlatinal often, begin with hematuria or strongly blood-tinged urine. When hematuria is profuse, this is a rare complication of acute uncomplicated nephritis and leads to profound anemia; the condition may become grave (See Hematuria, Section VI, III).

In children complete suppression of urine is much better borne during varying periods than in adults. This is particularly true of scarlatinal nephritis (See Uremia).

An abundant urinary secretion is the most favorable prognostic feature of acute nephritis in the presence of a sufficient heart. It therefore follows that markedly reduced renal function and cardiac weakness are the leading unfavorable features of acute nephritis.

Rapid heart early, with evidences of dilatation and edema, which is not favorably influenced by treatment within from three to seven days, is unfavorable. Rapid *heart arising suddenly* during the course of the complication with or without fall of systolic blood pressure, demands cautious watching and is often serious. If the pulse remains rapid and the systolic blood pressure is progressively lower and the pulse amplitude is low, myocardial weakness may be suspected and the prognosis should be guardedly offered. The condition is serious.

Heart weakness which is not improved by treatment, including rest and persistence of dropsy with stomach symptoms (vomiting-uremia) is always unfavorable.

The left heart is not likely to show marked hypertrophy during the early days of acute nephritis; rapidly developing enlargement of the heart with corresponding rise of systolic blood pressure demands close watching. Marked difference between systolic and diastolic pressure under such conditions, i. e., high pulse pressure, is suggestive of marked obstruction within the renal circuit. *Marked and persistent hypotension* is always serious. When with symptoms of acute nephritis there is within the first few days or weeks marked *hypertension* it may be safely concluded that the kidney lesion is not acute, that there is an acute exacerbation of a preceding chronic nephritis, and the prognosis must be shaped accordingly.

Sudden acute dilatation of the heart is an occasional fatal complication; this may follow with general edema and serous dropsies in cases with myocardial degeneration.

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Pulmonary edema with weak heart, unless it yields promptly, is usually fatal. With heart weakness pulmonary edema is likely to recur; with endo- and pericarditis it is always grave. Deep and persisting cardiovascular changes with acute nephritis are so rare that when present they excite a strong suspicion of subacute or chronic nephritis and the prognosis should be made accordingly.

Dropsy is by no means an expression of the severity of the acute nephropathy; it is the most constant symptom of acute nephritis. The pneumococcus, diphtheritic and typhoid nephropathies are rarely associated with dropsy, whereas the scarlatinal and syphilitic forms are likely to show dropsy.

There are innumerable chronic cardiopathies which develop in the wake of acute and neglected nephropathies.

Acute nephritis may complicate acute or subacute infections without causing symptoms of sufficient prominence to create a suspicion of its presence. Neglected, this may lead to chronic degenerative changes, i. e., chronic nephritis. *Acute nephritis, in spite of the disappearance of albumin and casts from the urine, may insidiously lead to subacute disease which finally merges into chronic and incurable nephropathy.* This is often true of the acute tubular nephritis of scarlatina, grip, diphtheria, tonsillitis, pneumonia and other infections.

Uncontrollable vomiting with cardiac weakness is always suggestive of uremia and unfavorable.

Vomiting during the early days of nephritis with or without febrile movement is not always serious; if it persists with reduced urine output and rapid pulse it is ominous.

Peritonitis with complicating nephritis, whether surgically or medically treated, is always exceedingly grave. *Appendicitis complicated by acute nephritis early* is usually deeply toxic; it is likely to be perforative and consequently grave. The sudden development of acute nephritis during appendicitis, whether medically or surgically treated, adds an enormous element of danger.

An occasional trace of albumin with the infections without elements in the urine, which justify the diagnosis of an acute nephritis, demands close watching but it is by no means of serious import (See Albuminuria).

Uremia is always a grave complication of acute nephritis but of much less serious import than with the chronic types of the disease. Barring scarlatina and diphtheria, deaths from uremia in uncomplicated acute nephritis are exceedingly rare. *In all cases the nitrogen content of the blood offers valuable prognostic data* (See Section VI, Anomalies of Urinary Secretion [1]).

As already suggested children often bear uremic poisoning longer than do adults, and complete suppression in children with toxic and infectious nephritis may continue during several days without a fatal issue (See

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Uremia). The *tolerance* developed by adults and children which makes it possible for them to withstand long periods of urinary suppression or marked reduction is surprising and in cases which often appear threatening the prognosis may justly include this encouraging feature.

The persistence of albuminuria after the disappearance of acute symptoms and dropsy, must lead to the suspicion of permanent renal damage—*chronic nephritis.* There are cases in the experience of all who watch their acute nephritics in which albuminuria in small quantities, without more than an occasional cast, persists during many months in which it occasionally happens that full recovery follows. The prognosis of such cases can be safely offered after thorough and repeated microscopic examination of the urine, blood pressure study and the physical examination of the cardiovascular organs.

The Blood.—Most cases present the *blood picture* of secondary anemia. The hemoglobin is markedly reduced; the erythrocyte count is low. The specific gravity of the blood is also reduced—in some cases to 1,020 or even lower. Increasing anemia with unfavorable urinary conditions and constitutional anomalies are often suggestive of subacute or chronic nephritis.

Anemia which persists after the disappearance of dropsy and the other acute symptoms must lead to thorough watching of the case.

If the specific gravity of the urine falls, the blood pressure rises and there is slight dyspnea on exertion and there is malaise in spite of the absence of albumin from the urine, subacute or chronic nephritis should be suspected.

When there is persistence of elevated blood and pulse pressure, accented second aortic sound after the disappearance of the dropsy and other acute symptoms, the patient has not been cured of nephritis; the case was either one of acute exacerbation of a preceding nephritis or consecutive subacute or chronic nephritis resulted.

Duration.—It is exceedingly difficult to give an accurate estimate of the duration of the acute nephropathies in favorable cases, for there is no assurance that there is return to a normal condition of the kidney tissue with the disappearance of all subjective and objective features. It often happens that months after the patient is supposed to be normal there are evidences of chronic nephritis which followed insidiously. The average case runs its course in from ten days to almost as many weeks. Cases in which many symptoms develop promptly—during the first week—are usually serious and likely to prove fatal. I agree with Tyson and Fussell that no cases which recover "do so in a few days." Cases may drag during long periods and finally recover.

Mortality.—Favorable cases show increased urinary secretion and decreased cylindrinuria usually after a period of concentrated and dark-colored cast- and epithelial-laden urine, with improvement or disappear-

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ance of the dropsies and the return of stomach tolerance which indicates improved urea elimination. But comparatively few patients die as the direct result of acute nephritis; it is a curable disease; even the more severe types are likely to recover. It should be remembered and it cannot be too often repeated that following the acute symptoms a remnant of latent nephritis may lead to chronic changes (chronic tubal or parenchymatous nephritis), which is incurable. The mortality is between 8 and 14 per cent.

Between 45 and 50 per cent of all acute nephropathies make a satisfactory and full recovery. The remaining 50 per cent pass into a subacute or chronic condition, markedly improve for a time or they die, usually of uremia (eclampsia), or cardiac insufficiency or some one of the complications mentioned in this chapter during the height of the disease.

The prognosis of the individual case depends more upon the cause of the nephritis—the underlying and primary disease—than upon the kidney complication itself; the toxemia of the former determines the malignancy or benign character of the latter.

Complications.—With *pneumonia,* either in the adult or during early life, febrile albuminuria is not always serious. Acute nephritis fully developed with pneumonia during the height of the disease is a part of existing deep toxemia, and is serious. If in these cases there is active delirium, many casts, reduced secretion, or with cardiac weakness and even limited infiltration of lung—such complications exist—they are always alarming (See Pneumonia—Section I).

Edema of the lungs has been considered in connection with the study of the prognostic significance of individual symptoms. It is always serious. It usually means *cardiac insufficiency.*

Peritonitis complicating primary nephritis is always grave and usually fatal.

High fever with correspondingly rapid pulse, which persists after the first six or seven days is usually due to some complication and is serious in accordance with its cause. The majority of acute nephritides are without marked elevation of temperature.

Purulent serous effusions (*empyema, pericarditis*) are always grave and add an enormous element of danger. I have referred to the other possible complications—heart and vascular anomalies—hypertension, and gastro-intestinal lesions, in connection with the consideration of the prognostic significance of separate symptoms.

Nephritis of Pregnancy

Kidney of Pregnancy

Albuminuria of Pregnancy.—As a rule, the albuminuria of pregnancy, is an expression of a degenerative and inflammatory nephritis

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with varying albumin loss, abundant casts, at times but few constitutional symptoms, in most severe cases edema, reduced urine output, retained nitrogen—the quantity varying with the severity of the lesions—often circulatory and ocular symptoms; in threatening cases there is uremia and nervous manifestations, including convulsions, etc.

With acute nephritis of pregnancy, I have relied upon the *daily measure of the urine secreted and the urea output to offer indications for treatment and prognosis;* such observations are possible in practically all cases away from the larger laboratories where naturally the other refinements of diagnosis (nitrogen and ammonia coefficient) are made.

The acute nephritis of pregnancy is much more likely to have associated uremia and ocular changes (retinitis) than does acute nephritis due to other causes.

Modern methods of diet and treatment have reduced the mortality of puerperal nephritis. Cautious watching of the nitrogen output and the nitrogen content of the blood, a cautious observation of the specific gravity, urea loss and subjective symptoms as pregnancy advances, make it possible for the obstetrician to prevent uremia and consecutive convulsions in most cases. There are now but few cases (exceedingly rare) of uncomplicated nephritis of pregnancy (albuminuria) which are not safely piloted through confinement, for the prognosis without eclampsia (convulsions) is not bad, and this complicates less than 25 per cent. The mortality among those who develop convulsions depends largely upon the care given and prompt rational treatment. The mortality of mothers with convulsions varies between 10 and 25 per cent. In some lying-in hospitals where these patients have received treatment (dietetic) during varying periods preceding confinement, convulsions are rare and the mortality among those who have them, because of prompt treatment, is low. *Convulsions are always serious; for the fetus the mortality is higher than for the mother*—reaching over 50 per cent.

Eclampsia.—The prognosis of eclampsia is more favorable when it occurs after than before delivery. Some obstetricians, however, report a high mortality after confinement. Olshausen and Lichtenstein lost 25 and 27 per cent of their cases respectively. Veit in 902 cases found the mortality among primipara 14.3 per cent and 19.1 per cent among multipara, while Goldberg and Lichtenstein claim that eclampsia is most dangerous in multipara, while Olshausen found no difference in the two groups.

With persistently high systolic blood pressure and convulsions the outcome is serious. Anuria unrelieved after a reasonable period, inability of the patient to sweat in a hot pack (Williams), pulmonary edema, feeble, rapid and small pulse, are unfavorable.

With the death of the fetus or its expulsion, the danger of further convulsions is materially reduced. With chronic nephritis and pregnancy

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there is always great danger of recurring convulsions and uremia. The cases which offer a serious prognosis are those which develop suddenly—usually late—in which the toxemia is at once overpowering and uremic convulsions are the first indication of any disturbance.

Eclampsia arising suddenly toward the end of pregnancy in untreated and unsuspected cases in which convulsions continue after delivery, often with suddenly arising dropsies, offers an unfavorable outlook.

Suddenly arising general dropsy with marked reduction of the urinary secretion and lowered renal sufficiency toward the end of pregnancy, with or without convulsions, is always ominous.

The prognosis is grave in those cases in which there are early *retinal hemorrhages;* in some of these the acute nephritis is grafted upon a chronic nephropathy. *Retinal hemorrhage* in all cases of puerperal nephritis is an unfavorable complication, particularly when associated with convulsions. Many recover fully after puerperal retinitis after supposed retinitis has proved to be uremic.

Le Page after reviewing his experiences warns against the dangers of subsequent pregnancies and his statistics prove that the stricter medical advice is followed the more favorable will be the outcome. With systematic care, Le Page with others, agreed that later pregnancies can usually be carried to a successful termination. My experience is encouraging; warned by the original nephritis, subsequent pregnancies have, because of rigorous diet, rest and thorough surveillance, rarely, unless chronic nephritis was already fully established, given serious trouble; as a rule the unfortunate complication did not recur. With women who suffer from chronic nephritis, nephritic toxemia should be feared during pregnancy (Williams).

Pregnancy aggravates existing nephritis. With symptoms of fully developed chronic nephropathy the dangers are multiplied; the blood changes are often prompt, the accumulation of toxic material is increased; the added cardiovascular task invites insufficiency, and resistance is consequently reduced.

In our experience the "kidney of pregnancy" occasionally serves as the cause of chronic nephritis. Such cases finally follow the clinical course of the ordinary parenchymatous disease. One of my cases lived over twenty years after her initial nephritis in which she had eclampsia and transitory blindness and died after a long period of hypertension, hypertrophied heart and arterial degeneration in coma.

When face to face with the kidney of pregnancy the prognosis must be cautiously given and the case always demands the closest surveillance. *Eclampsia is always to be feared; the time of occurrence cannot be foretold in the individual case; it is the leading danger, and prognosis remains uncertain until the time of its possible occurrence has been safely passed.*

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(*b*) *Chronic Parenchymatous Nephritis*

(Chronic Bright's Disease, Chronic Tubal Nephritis, Chronic Glomerulonephritis, Chronic Diffuse Nephritis, Chronic Catarrhal Nephritis, Chronic Nephropathy, Large White Kidney)

General Considerations.—Chronic nephritis is a progressive and productive disease of the kidney most frequent between the ages of twenty-five and forty, in which the organ is at first enlarged (*large white kidney*) with a chronic diffuse hyperplasia involving the epithelium, the glomeruli and the interstitial tissue—always a grave condition—offering an absolutely bad prognosis for restitution to health. In all, there is a marked tendency with the productive changes to final atrophy (*secondary contracted kidney*). Besides these changes the *cardiovascular system* is involved early and the *blood pressure* is elevated to compensate for the renal obstruction that the tissues of the body may receive the needed food. There is never complete regeneration of destroyed kidney tissue; new tubules are never formed, neither are new glomerules reformed after their destruction. It is possible for epithelial cells to proliferate when neighboring single cells have been destroyed, provided always that the tubular structure has remained intact.

With destructive changes in the kidney both glomerules and tubules may undergo compensatory hypertrophy in the organ involved. These compensatory changes in diseased kidneys, the same as is found with enlargement of the remaining kidney following the destruction or removal of its fellow, are among nature's processes which make it possible for the kidney—when not too extensively diseased—to continue to perform sufficient function to maintain life during long periods in individual cases. For prognosis this fact is of transcendent value and is true of all forms of nephritis. *With the chronic nephropathies life is often continued during many years in comparative comfort because of the reserve and compensatory power of these complex organs.* We can easily spare, as Bradford contends, two-thirds or even more of our kidney substance without serious inconvenience.

In practice I have never seen a true case of chronic tubal nephritis make a full recovery. Those cases which have been reported cured were either the extended form of acute nephritis, often syphilitic nephritis, or the diagnosis was not absolutely correct.

The majority of all cases are far advanced when they present for treatment. The disease is insidious very often without offering many subjective or objective symptoms. In some cases there is from the beginning a combination of interstitial and glomerular nephritis, with prompt cardiovascular change, including high blood pressure. Such cases are likely to show dropsies and uremia, while myocardial degeneration and the

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attending symptoms usual with broken compensation are in the foreground early; this combination is promptly threatening and fatal early.

Origin.—It is often exceedingly difficult, almost impossible, to be sure of the cause of chronic nephritis. In considering the acute nephropathies, I mentioned the possibility of chronic nephritis as a cause; Tyson believes that "more frequently it originates *de novo*."

Prognostic Features

Cases which follow the nephritis of scarlatina and pregnancy never recover, though they may live many years with but few symptoms so long as there is compensation within the cardiovascular system and uremia or other complications (infections particularly) are prevented.

Cases which owe their origin to cold or exposure in which the cause is repeated are likely to progress and are subject also to lung complications.

Malarial infection may lead to chronic and fatal nephritis, though in this country it is less frequent than in Germany and other countries. Thayer in his Johns Hopkins Hospital experience found that of 1,823 cases of malaria 25 had nephritis.

Prolonged surgical (pyemia, sepsis and tuberculous) **conditions** causing or associated with parenchymatous nephritis argue against the prolongation of life.

Nephritis due to chronic lead poisoning is always associated with cardiovascular changes, usually marked arterial thickening and hypertension. When the condition is discovered early, exposure to lead is prevented, the kidney lesions and arterial and heart anomalies are incipient, the process may remain latent during many years and never progress; such patients may ultimately die of intercurrent disease. Chronic or advanced lead poisoning in which the kidney is involved, in which the associated cardiovascular changes are also marked, offers an absolutely hopeless forecast and the length of life depends upon a number of factors —ability of the heart and arteries to compensate, the prevention of rupture of the changed arteries, the renal sufficiency, the prevention of uremia, the addition of complications referable to the lungs and brain, and a number of other conditions which may arise early, often without warning.

Retinal hemorrhage with *saturnine chronic nephritis, whether largely of the mixed type or interstitial, is always unfavorable*—such patients usually die within twelve months; they rarely live more than from eighteen to twenty-four months.

Persistent or recurring digestive derangement *is always unfavorable —most of these are due to chronic uremia.*

Recurrent and uncontrolled vomiting *is always grave.* With reduced

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urinary secretion and digestive disturbance the prognosis is bad, whatever the renal sufficiency test may unfold.

Progressive and unrelieved anemia is evidence of profound toxemia and is usually associated with edema, hypertrophied and weak heart and the usual blood pressure changes. Caution in prognosis is needed when in spite of the relief of the dropsies the anemia persists, for such behavior is unfavorable for the prolongation of life during a long period.

Marked myasthenia is always unfavorable; when this is associated with dyspnea or orthopnea the end may be expected at any time, though such symptoms with or without uremia may at times be relieved during limited periods, but they are likely to recur.

Uremia.—I have fully considered the prognostic significance of uremia under Anomalies of Urinary Secretion (d) of this Section, to which we refer the reader for a full consideration of the subject.

It should be remembered by the clinician that many nephritics live during long periods without sufficient uremia to cause alarming symptoms. It is possible for uremia to become overwhelming suddenly, to cause deep disturbance of the central nervous system—convulsions or coma—by which the life of the patient is threatened. Many die without regaining consciousness. On the other hand *the patient may rally from profound uremic poisoning, the sensorium may clear, the heart function may prove sufficient to assist the patient into a period of material improvement, making it possible for life to be prolonged and usefulness continued during limited periods. From the medicolegal point of view it is exceedingly important to remember that deep coma and clouded brain function may disappear and the patient may fall into a condition of chronic uremia in which the brain function continues to be normal. Chronic uremia in such cases includes gastro-intestinal symptoms and lethargy, but judgment is not clouded in the majority of cases. With chronic nephritis such occurrence is not uncommon; sooner or later the symptoms of deep uremia return unless the patient loses his life as the result of some complication, usually cardiac.*

There are chronic parenchymatous nephritics who live comparatively comfortable during years, who are almost continually slightly uremic. This condition in such subjects shows itself with gastro-intestinal symptoms, often high blood pressure, in the stage of secondary contraction, abundant urine, increased nycturia, hypertrophied left ventricle and persistent but slight anemia. They usually remain sufficiently active mentally to attend to their business, and in many cases their executive ability has not been reduced. *The coma of nephritis may recur after short intervals during which the patient may be either clouded mentally or he may return to full consciousness.*

Prolonged drowsiness, uncontrollable insomnia or other evidences of invasion of the nervous system are among the evidences of uremia which

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are common in advanced nephritis, and with other symptoms of progression argue against the prolongation of life.

Once uremic, the chances are that recurrence will not be long postponed in the majority of cases. This is not without many exceptions, for months and years may pass without toxemia after eclampsia and deep coma.

Renal Sufficiency Test.—Where there are sufficient laboratory facilities in connection with the test for renal sufficiency the examinations for retained nitrogen by the Folin method or other methods, which are held by some laboratory workers to be more efficient, may be made (See Renal Sufficiency Tests, Section VI).

In normal subjects the *residual nitrogen* in the blood amounts to about 50 mgms., while in uremia it may rise to 250 mgms. When 150 mgms. are reached the prognosis is grave; from 50 to 75 mgms. has no prognostic significance; from 75 to 150 mgms. is not without hope (Strauss).

Dropsy.—Dropsy is a leading symptom of chronic nephropathy, present in 90 per cent of cases. It is never to be lightly considered prognostically. With chronic tubal nephritis it is less likely to be a symptom of the terminal stage of the disease than with interstitial nephritis or the secondary contraction of the former.

In the early stage of the disease the disappearance of dropsy under treatment is not unusual. Irregularly distributed dropsy, sometimes greater on one side or in one member than in the other, is quite characteristic. Marked edema of the genitals in both the male and female may be early or late. Any form of dropsy with chronic nephritis, particularly when associated with marked cardiac insufficiency, with reduced urinary secretion, retained urea and with fluid in the serous cavities, is unfavorable for the prolongation of life.

In the stage of secondary contraction and unfavorable urinary features the conditions mentioned in the preceding paragraph are rarely relieved.

In offering the prognosis of chronic nephritis in the presence of extensive dropsy, *insufficient cardiac force, hydremia and vascular changes are paramount.*

Many neglected hospital cases of chronic tubal nephritis with extensive dropsies have been successfully treated, i. e., the dropsy has been relieved and life has been prolonged—but sooner or later these patients returned with exacerbation of the original symptom.

Urine.—The urine of chronic nephritis offers positive prognostic data. *Abundant urine* with specific gravity at normal or slightly above, but moderate debris, occasionally hyaline, few granular, mainly epithelial casts and moderate epithelial desquamation with considerable albumin is not alarming. So long as the specific gravity and amount of secreted urine

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remain within normal limits, the number of casts is limited and without evidences of advancing degeneration in abundant granular and fatty casts, other symptoms (objective and subjective) are favorable, the prognosis for life is good.

When the specific gravity begins to fall, the quantity of urine secreted is increased, the urea and nitrogen of the blood are also increased, the quantity of urine voided during the night equals or exceeds the quantity of the day, with or without dropsy, it is safe to conclude that the atrophic stage is fully established. Lowered urea output in this stage with progressively increasing gastro-intestinal symptoms, hypertension and increasing heart changes (hypertrophy, dilatation, myocardial degeneration) and dropsy, offer the complex of the terminal stage of most chronic nephropathies. Marked lowering of the urinary secretion with general dropsy (anasarca), loss of functional ability of the kidney as shown by the phthalein test or urea estimation is unfavorable. Marked delay in the excretion of potassium iodid is unfavorable.

The clinician should never depend on renal sufficiency tests alone for prognosis (See Renal Sufficiency Tests, Section VI, Anomalies of Urinary Secretion (e)).

Paroxysmal hematuria (See Hematuria) with chronic tubal nephritis is usually indicative of progression and vascular degeneration, though there are cases in which hemorrhage recurs after exposure to cold during many years. With such cases hematuria may not return more than once in two or three years. I recently saw an active lawyer, aged 43, who since his sixteenth year has had repeated attacks of hematuria (average of 3 or 4 each year); on one occasion, 12 months before the consultation, he had uremic convulsions. All physical signs and urinary features are characteristic of chronic tubal nephritis. He is mentally alert and has recently been elevated to the bench. Such cases usually show high systolic pressure, but this was not present in the case mentioned, for there were evidences of myocardial weakness with systolic blood pressure —120 mm. Hg. The urine showed both hyaline and granular casts with moderate albuminuria, specific gravity 1,017, acidity 20°. Such symptoms are a continuous menace but the patient may live many years. *The dangers are sudden uremia with anuria; chronic uremia with prompt increase of vascular disease, cerebral hemorrhage. Edema of the brain or lung may end the scene.*

Blood Pressure.—The significance of blood pressure study and hypertension as prognostic features has been fully considered in Section III (See Section III—Arteriosclerosis).

Hypertension is characteristic of chronic nephritis; it is not long postponed after the symptoms of the nephropathy are positive and it may occasionally precede other diagnostic features of the disease.

Once the hypertrophy of the left ventricle is advanced and hyperten-

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sion is striking, the disease may be considered fully established and progression is the rule.

Hypertension and hypertrophy are compensatory and salutary, the fall of the former and the failure of the latter (dilatation) argue in favor of degenerative change in the myocardium, increasing weakness, and with other evidences of cardiac insufficiency (dyspnea, orthopnea, dropsies) a fatal termination may be presaged. Low systolic pressure with a high diastolic pressure, hence a small pulse pressure, is characteristic of the myocardial weakness of nephritis. High systolic pressure and low diastolic pressure, hence a large pulse amplitude, are characteristic of chronic nephritis before the break. In the study of advanced nephritis a small pulse amplitude is evidence of cardiac insufficiency. Gradual or sudden fall of systolic blood pressure after a period of hypertension is always significant of failing compensation and calls for an unfavorable or guarded prognosis.

Coronary disease with chronic nephritis, **repeated attacks of angina pectoris,** makes the prognosis exceedingly grave (See Angina Pectoris, Section III).

Pulse.—*Changes in the character of the pulse and pulse rate to correspond with the fall of systolic blood pressure and lowered pulse amplitude offer valuable data for prognosis; in all stages of chronic nephritis—particularly the atrophic—such changes are positively unfavorable.*

Alcohol, Proper Living, Etc.—The prognosis of chronic nephritis is clouded by the persistent use of alcohol and the failure of dietetic, medical and climatic treatment with cautious living to control the symptoms. It is surprising to note how fully established nephritis, often in the stage of secondary contraction, remains stationary during long periods under favorable conditions and scientific diet.

Edema.—My experience is in accord with Francis Boyd's who says that "edema may be due to salt retention; but salt retention may be combined with degenerative changes in the smaller vessels and with cardiac failure." When the salt-free diet reduces existing edema and increases the urinary flow the prognosis for prolongation of life is favorable. The edema due to cardiovascular degeneration is rarely favorably influenced by the salt-free diet alone; in connection with digitalis and theobromin salicylate I have experienced satisfactory improvement during long periods.

Arteriosclerosis and Faulty Living.—In *active brain workers* with associated arteriosclerosis and faulty living, with unchecked activities the progression is often surprisingly rapid, and death may follow before the end of twelve months.

Heavy responsibilities add enormously to the dangers, invite uremia and rapid cardiovascular failure, while rest under favorable surroundings often prolongs life during periods of surprising length.

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Retinal Changes.—Retinal changes in the subjects of chronic nephritis are of considerable prognostic significance. Patients with albuminuric retinitis (hemorrhage) rarely live beyond two years, often not so long. One-half of my cases died within one year of the diagnosis of the complication. Nettleship found that in 42 cases "one-fifth only of the cases lived for more than two years, and no less than 25 died within the year from the time of the recognition of the ocular changes (Bradford quotation of Nettleship statistics).

Complications

Most complications of all chronic nephropathies are due to added infection. Following *surgical operations* infection is frequent, while resistance to the operation itself is lowered and the prognosis is bad (See the Infections—Section I).

I have called attention to the dangers of pericarditis, pleuritis, empyema, pneumonia, endocarditis, peritonitis, bronchitis and diseases of the stomach and intestinal tract in the various sections of this book (See the Infections, Section I, and Diseases of the Pericardium, Section III, etc.).

With all of these complications, if the nephropathy is advanced or secondary contraction is established, the prognosis is grave and should be given with reserve. Pericarditis is particularly unfavorable as a complication. Cerebral apoplexy with chronic nephritis is always serious; restoration of brain function is rare; death in coma has been the rule in my cases.

Acute meningitis is usually preceded by a period of cerebral symptoms (headache and mental torpor); the course of the disease is progressive and death is the rule (See Meningitis). (The reader is referred to the Pneumococcemias and Pulmonary Edema, also the other respiratory diseases for further data concerning their prognostic significance when complicating nephritis).

The frequency of *duodenal ulcer with chronic nephritis* has been overlooked by most clinicians (See Ulcer of the Stomach and Duodenum, Section V). The dangers are perforation with final peritonitis, also subphrenic abscess (Barie et Delauney, Dickinson).

Purpura, visceral symptoms with *erythema* and *nephritis* often prove serious complications (Henoch, Osler).

Conclusions

Conclusions based on the preceding data prove chronic parenchymatous nephritis to be a grave disease which is never cured. Cures and long latent periods have been reported but *restitutio ad integrum* has never been demonstrated.

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The duration of the disease in comparative comfort during many years is often surprising and this may occasionally follow a period of threatening symptoms including uremia. Prompt, early recognition, rational treatment and living, often prove of great importance in prolonging life and favorably influencing the course of the disease.

Unfavorable features leading to death are sudden uremia, persistent dropsies and uremia with cardiovascular changes including myocardial degeneration, retinal hemorhage, the complications (surgical and infectious) mentioned in the preceding pages, recurring hematuria and profound anemia with myasthenia. Surprises are in store for the clinician; cases which at times seem to progress favorably are suddenly and unexpectedly overwhelmed by uremia or some other complication; while with almost equal frequency a serious symptom complex may mend and life may be indefinitely prolonged. There are no set rules for the prognosis of any of the nephropathies; all require the close study of the individual case almost continuously.

Surgical Treatment and Prognosis

In spite of the rose-colored prognosis offered by Edebohls following his introduction of surgical interference in chronic parenchymatous and interstitial nephritis (decapsulation of the kidney) the profession of this country and of the continent of Europe found no justification for its recommendation. Results have been unfavorable—at times immediately disastrous. There are a few cases in which pain is prominent with persistent anuria and dropsy, in which splitting the capsule may be indicated. In these the tension of the capsule is great and its splititng gives relief.

(c) *Chronic Interstitial Nephritis*

(Contracted Granular Kidney, Fibrosis of the Kidney, Contracted Kidney, Red Granular Kidney, Gouty Kidney, Arteriosclerotic Kidney, Chronic Nephropathy, Renal Cirrhosis, Renal Sclerosis, Granular Kidney, Senile Kidney)

Leading Features.—The leading features of chronic interstitial nephritis are progressive destruction of the tubular apparatus of the kidney, change in the arterioles of the organ, interstitial overgrowth and atrophy.

Various Forms.

First Variety.—The last stage of chronic parenchymatous nephritis leads to atrophy of the kidney or *"secondary contracted kidney"* in which there is marked productive change which has justified some to consider such kidneys as belonging to the chronic interstitial type (See Chronic Parenchymatous Nephritis).

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Second Variety.—There is a second variety of interstitial nephritis which may be considered primary, known as the *"contracted kidney" or "red granular kidney."* This variety may be due to one of several causes, including gout, lead, alcohol, syphilis, errors of diet long continued, and very often, hereditary influences.

Heredity.—With a strong hereditary taint the prognosis for life of the arteriosclerotic kidney is less favorable than without it. My histories show that with several members of a family (brothers and sisters) suffering from nephritis the disease is almost always of the arteriosclerotic type, that grave vascular complications are frequent, including apoplexy, that cardiac stability is uncertain, metabolic faults—such as diabetes and gout—add to the dangers, and that angina pectoris is comparatively frequent and fatal.

Third Variety.—The third variety of chronic interstitial nephritis is arteriosclerotic and is in all probability the most frequent type of the contracted kidney, for there are but few cases of chronic interstitial nephritis, in which the arterioles are not sclerosed. It is this form of chronic nephritis in which the kidney changes, so far as the arteries are concerned, are a part of a general degeneration and productive process involving the blood vessels throughout the body.

Fourth Variety.—The fourth type has been characterized by Osler as the *"senile form."* It is the *contracted kidney of old age* in which the organ is reduced in size, with thickened and adherent capsule, increased pelvic fat and marked atrophy of the pyramidal and cortical substance, with prominent arteries throughout the kidney (Osler).

Outlook.—The prognosis of contracted kidney must be based upon the leading underlying pathologic condition, i. e., disease of the arterioles through the entire body, including the organ under consideration.

The disease cannot be cured. Detected early it may by proper care be held in abeyance. Even this is doubtful, but is in accord with the observations of some excellent clinicians (Senator). While interstitial nephritis is an incurable disease, its presence is by no means inconsistent with long life in many cases when compensation of the cardiovascular tree is sufficient and renal function is but little disturbed. Such patients may live in comparative comfort during many years. All clinicians of experience constantly number among their patients chronic nephritics who by practicing temperance, sobriety and abstinence, are without the knowledge of the dangers which surround them or the changes in heart and arteries which are necessary to compensate for existing faults.

Prognostic Features

The prognosis therefore of all varieties of interstitial nephritis depends primarily upon the ability of the heart to compensate for the resistance

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within the renal circuit and periphery, the security of the arteries, and the ability of the kidney to functionate sufficient to prevent uremia. Much depends therefore upon the co-operation of the patient and his ability to regulate his daily life.

Blood Pressure and Heart Changes.—Blood pressure study of chronic interstitial nephritis and changes in the heart have been fully considered in the treatment of *hypertension, arteriosclerosis, myocardial disease* and *chronic nephritis* (the latter in this section).

Blood pressure must of necessity be elevated and the heart enlarged to overcome arterial resistance and renal block. The *hypertension* of interstitial nephritis and the *pulse pressure* are higher than with chronic tubular nephritis, but the prognostic data in both are practically identical and do not require repetition, though apoplexy is more frequent with the interstitial disease. In both, sudden or gradual fall with attending symptoms of increasing circulatory embarrassment is ominous. Many cases of chronic interstitial nephritis present for treatment only after there is a *break of compensation with dropsy,* dilatation of the heart, often *pulmonary edema, orthopnea* and *other terminal symptoms.* These patients die of *cardiac asthenia.*

Renal Insufficiency.—Another class of patients suddenly or gradually develops the positive symptoms of *renal insufficiency.* The kidney function materially reduced, toxic symptoms follow, uremia—either acute (eclampsia) or chronic—becomes life-threatening, persistent vertigo incapacitates the nephropath, and not infrequently cerebral hemorrhage or sudden cardiac dilatation add to the danger and end life.

Persistent or recurrent headache with marked hypertension, thick artery (radial) and ocular disturbances may continue during several weeks or months, but when these symptoms are uncontrolled by treatment or rest, serious complications—either cerebral apoplexy or uremia—may be expected. It not infrequently happens that unrecognized nephritis ends without warning with cerebral apoplexy or sudden overpowering uremia. In some of these cases, particularly in the uremic, occipital headache may precede the end during several days (Seguin).

Marked hypertension with hypertrophy of the left ventricle may continue during many years with chronic interstitial nephritis and not materially interfere with the life of the patient. I have had such a case under observation during almost ten years: a woman, aet. 52, who during that time has never had a blood pressure below 250 mm. Hg., with enormous hypertrophy of the heart, who until within the past month has been able to teach in a country school but who is now showing evidences of increasing peripheral resistance. The blood pressure is so high that it cannot be accurately measured by any instrument at our command, the pulse amplitude is correspondingly high while evidences of chronic uremia and cerebral arteriosclerosis are increasing.

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Polyuria, nocturnal frequency, cerebral symptoms (headache, vertigo and visual disturbances) **with hypertension** in patients below fifty years of age always makes the prognosis serious; most of these nephritics die of uremia.

Dyspnea—Orthopnea.—It matters little what the urinary picture is when with hypertension early, there is dyspnea or orthopnea; for these are evidences of *cardiac insufficiency* and make the outlook dark. Marked accentuation of the *second aortic sound* (almost constantly present) *with increasing hypertension and irregular or arhythmic heart is a discouraging complex.*

Stasis.—The *break in compensation* often follows a period of increased tension; the artery is evenly thickened, like a "pipe stem" under the finger. *The suddenly appearing irregularity, intermission or other anomalies of the pulse when promptly associated with respiratory embarrassment or other symptoms of stasis are always unfavorable.*

Intermittent or irregular hearts which have become chronic and which are not due to advanced myocardial degeneration may not interfere with the comfort or the life of the patient during unlimited periods. Such hearts, however, when facing an added burden are likely to prove insufficient.

Sudden tachycardia is serious; when associated with dilatation there may be *pulmonary edema with* general *anasarca.* These paroxysmal attacks repeat themselves at short intervals in cases with myocardial degeneration.

Adams-Stokes phenomenon is a part of the far-reaching arteriosclerosis. **Angina pectoris** may complicate chronic nephritis and makes the tenure of life uncertain (See Angina Pectoris).

Respiratory Symptoms.—Respiratory symptoms, particularly bronchitis, with nocturnal dyspnea and occasional bloody or pinkish expectoration are suggestive of final fatal edema of the lungs.

Orthopnea with dropsy (a late complication) is soon followed by death. *Cheyne-Stokes breathing* is a terminal symptom.

Dropsy.—Dropsy is not an early symptom of the average contracted kidney. There may be transitory edema of the ankles but fully developed dropsy is a terminal complication and depends upon broken compensation.

Dropsy with ocular symptoms does not continue long before death.

The same general conclusions given in the consideration of chronic tubal nephritis in its advanced stages with dropsy may be accepted for the prognosis of contracted kidney (See Chronic Parenchymatous Nephritis).

Edema of the glottis with all forms of nephritis is a serious complication and demands immediate surgical treatment when it causes respiratory embarrassment.

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Digestive Symptoms.—Symptoms referable to the digestive system are always suggestive of uremia and should be so interpreted for our purposes.

Vomiting not dependent upon error of diet is either of uremic or cerebral (arteriosclerotic) origin and demands cautious consideration, for it is usually unfavorable.

Diarrhea is often salutory and should be so considered in most cases by the therapeutist for it may be an expression of existing uremia; occasionally it is profuse, weakening and unfavorable.

Persistent constipation or obstipation may lead to threatening toxic symptoms and for safety demands rigorous treatment.

Urine.—The urine offers prognostic data of considerable importance. During the stage of full compensation when conditions are favorable and the disease is not far-advanced, the quantity is decidedly increased, the specific gravity is low, the albumin loss may be slight or so small as to escape detection with ordinary tests; there may be no casts or only an occasional hyaline cast; the urea is decreased but not always strikingly so; nocturnal frequency is slightly increased but the quantity is not so great as in the advanced stage; the functional tests are favorable. The occasional red blood corpuscle, a few renal cells, an occasional leukocyte and squamous epithelia are frequent and not of great significance when there are no untoward complications or associated symptoms.

When the nocturnal secretion of urine is greater than the diurnal and with this there are other evidences in increasing systolic pressure and heart changes of greater renal obstruction and the radial artery shows increasing arteriosclerotic change (thickening increasing), there are usually gastro-intestinal and pulmonary anomalies—all of which argue in favor of an early break.

Probably there are but few cases of chronic interstitial nephritis which are not *non-albuminuric* during varying periods. *There are many cases of non-albuminuric nephritis which are easily recognized if the possibility of their existence is borne in mind.* It is often possible to diagnosticate and prognosticate this anomalous form of the disease, months before albumin or the usual features are established. *Many cases diagnosticated as hypertension without albuminuria have proved to be insidiously progressive interstitial nephritis.*

Hypertension in which the symptom is not due to aortic disease, in which the urine may contain no albumin or only a trace, no matter what the other associated arterial lesions may be is as a rule due to chronic nephritis and is progressive. If in the advanced stages the blood pressure is excessively high, the urine begins to show increasing albumin loss, the quantity secreted grows less, the cylindruria increases and urea detention is increased, the eye symptoms are prominent and the heart shows increasing weakness, death is imminent.

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It is not impossible in chronic nephritis after periods of markedly reduced urine secretion—almost complete anuria—to find the kidney function improved, and it may again prove sufficient during varying periods. Once the patient has lived through such a period he may be considered to be in constant danger of recurrence of renal insufficiency with attending uremia.

Anemia.—As a rule the anemia of chronic interstitial nephritis is less striking than with the other nephropathies. *Persistent anemia with myasthenia* is unfavorable and is usually associated with renal insufficiency—chronic uremia. In the terminal stage, with persistent dropsy and other threatening symptoms including increased urinary anomalies, the anemia is often profound. Anemia which has become chronic is unfavorable because it is an expression of one or more grave underlying conditions.

Albuminuric Retinitis.—What I hold in connection with the retinitis of chronic tubal and glomerular nephritis is also true of contracted kidney. Diffuse opacity due to edema, hemorrhage and optic papillitis are common, and are evidences of advanced arteriosclerotic nephropathy. *Once there is diffuse retinitis and hemorrhage the patient's fate is sealed and uremic or cardiac death may be expected at any time, though some of these patients live as long as two years after positive changes in the fundus of the eye.* Albuminuric retinitis is among the most valuable of prognostic data and often serves to strengthen the forecast in the absence of other reliable features. It may be the first recognized symptom to lead to the diagnosis.

Purpura is positive evidence of profound toxemia and lowered resistance and is usually a terminal complication.

Repeated epistaxis is always suggestive of arterial degeneration, usually advanced, and may be the first of a series of hemorrhages with final cerebral apoplexy.

In one of my cases there was first epistaxis, then urethral hemorrhage; these alternated with each other. Death was due to cerebral hemorrhage after a fishing excursion on an unusually hot day. Such experiences are not unusual.

Complications

The complications of chronic interstitial nephritis are practically the same as are those of the chronic parenchymatous disease and offer the same prognosis (see Chronic Parenchymatous Nephritis) though the arterial anomalies (cerebral hemorrhage) are more frequent with interstitial disease.

Surgical Operations and Infections

Surgical operations and infections are not well borne by the subjects of chronic arteriosclerotic nephropathies. This is particularly true of

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surgical operations on the genito-urinary organs and with pneumococcemia. With pneumonia, the pulse is at first reassuring, often slow, the tension slowly falls, and after a few days the heart muscle is exhausted. After bladder and prostate operations there is often prompt and sudden suppression of urine which with a failing heart leads to death.

Duration

The duration of this form of nephropathy is always uncertain. The patient is doomed but yet, as contended in the beginning of this chapter, the disease is by no means inconsistent with long life and in many cases the regulation of the habits and life of the patient makes it possible to add years of comparative comfort. Early recognition is an important favorable prognostic factor. I have had patients who have lived over twenty years with interstitial nephritis.

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(d) *Congested Kidney*

(Cyanosed Kidney, Hyperemia of the Kidney, Stauungsniere)

(1) Acute Congested Kidney

Whether acute or chronic, congested kidney is a *secondary condition*. Hyperemia of the kidney follows general stasis within the venous system; insufficient cardiac force, in which the kidney and other organs of the body are likely to be involved at the same time, or local pressure may cause this condition.

Acute congestion of the kidney may be associated with the *acute infections*. Whenever the circulation is impaired through the renal circuit or whenever cardiac weakness causes renal stasis from acute or suddenly arising complications, hyperemia results. Some have held that the kidneys are not congested during the acute infections but that they are

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anemic (Walter Mendelson). There is proof, however, that in most cases there is acute hyperemia. Turpentine, copaiba, cubebs, cantharides, arsenic, carbolic acid and other substances which also cause genito-urinary irritation may produce acute congestion of the kidney. *Heart lesions with acute exacerbations or sudden cardiac insufficiency from any cause may provoke, among other evidences of general stasis,* all of the urinary features of acute cyanosis of the kidneys.

Unquestionably there is in most cases of acute nephritis a period of congestion in which the kidney shows the characteristic changes of hyperemia. The prognosis of acute congestion of the kidney must always depend upon the nature of the primary cause and the ability of the therapeutist to overcome its grave secondary effect. The majority of cases of infection in which the urine shows the results of renal hyperemia, in which toxemia is not overpowering and the resistance of the patient is normal, recover fully. It should be remembered in offering the prognosis of acute renal congestion with the infections that the noxious effect of the toxins on the kidney is more important than any direct circulatory embarrassment (stasis).

(2) Chronic Congested Kidney

Causes.—The leading causes of chronic congested kidney are

(a) Heart lesions
(b) Pulmonary obstruction
(c) Local obstruction
(d) Venous stasis from whatever source.

(a) Heart Lesions.—The leading heart lesions which cause renal stasis are valvular and myocardial. The valvular defects are usually *mitral* or *tricuspid,* or both may be present. *With valvular disease or degeneration of the heart muscle (myocardial insufficiency)—usually during periods of broken compensation*—the symptoms of renal cyanosis are added to the others which together complete the picture of cardiorenal obstruction. With all of these primary anomalies the condition of the heart muscle and the ability of the congested kidney to prove sufficient remain the paramount prognostic features. There are often long periods of congested kidney with chronic valvular lesions and myocardial weakness in which rest and rational treatment improve conditions with the relief of venous stasis. As a rule, with chronic heart lesions cyanosed kidney is an expression of failing heart strength, and consequently only a symptom of a grave condition. Many of these patients with chronic heart lesions live for years during which, with temporary recurring loss of heart strength, there are repeated periods of congestion of the kidney. Rest and rigorous scientific treatment of the underlying heart lesions (if amenable to treatment) are important factors in prolonging life.

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(*b*) PULMONARY OBSTRUCTION.—Acute and chronic pneumonia, tumors of the lung and mediastinum (aneurismal growths, etc.), emphysema, and chronic asthma, pleurisy and pulmonary tuberculosis may cause renal stasis. Here too the prognosis depends entirely on the nature and extent of the primary lesion. We have fully considered the renal complications and their prognostic significance with each one of the primary diseases above mentioned.

(*c*) LOCAL OBSTRUCTION.—Local obstruction to the return of blood from the kidney associated with thrombosis, embolism—sometimes of the vena cava—compression of the renal vessels by abdominal growths, often cause stasis. Most of these conditions are serious.

(*d*) VENOUS STASIS FROM WHATEVER SOURCE.—Venous stasis from whatever source, not included in the preceding paragraph causing congested kidney is, as a rule, evidence of advanced disease. This is particularly true of the numerous diseases of the liver associated with portal obstruction (See Diseases of the Liver, including Cirrhosis, etc.).

General Statements

Long continued cyanosis causes productive changes in the kidney leading to connective tissue increase and consecutive contraction. These cases are associated with thickened renal vessels, and finally there are changes in all structure of the kidney (*diffuse interstitial nephritis*).

The *length of life* depends upon the ability of heart and kidney to bear the strain.

Congested kidney associated with other serious organic disease—malignant disease of the liver, Hodgkin's disease, pernicious anemia, aneurismal dilatations within the abdomen or elsewhere, is usually among the terminal manifestations. The symptoms are mainly circulatory, respiratory and renal.

The *prognostic significance of the symptoms* of the primary disease need not be reconsidered in this section; the reader is referred to the separate chapters dealing fully with the primary diseases.

The *urine of the cyanosed kidney* may be materially reduced in quantity, the specific gravity is high (1,025 to 1,035), dark colored, often cloudy. The amount of albumin is small. In the microscopic field there are red blood corpuscles, blood casts occasionally.

With congested kidney, the *disappearance of albumin and casts is coincident with returning heart strength—hence favorable.* Improvement of the circulation often runs parallel with change in the concentration of the urine; the specific gravity falls with increase in the quantity of the urine at the same time. The higher the specific gravity the greater is the engorgement, hence the smaller the quantity of the urine secreted.

Uremia is not to be dreaded in uncomplicated cyanosis of the kidney.

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They may exist within the urinary organs or without—*intrarenal and extrarenal.* The obstruction may be either *congenital* or *acquired.* It may be *unilateral* or *bilateral.*

Prognostic Factors

(1) *The cause of the obstruction*
(2) *Whether the lesion is unilateral or bilateral*
(3) *If unilateral, the condition of the second kidney*
(4) *The general condition of the patient and complications*
(5) *The time of recognition and the ability to treat the condition surgically.*

(1) The Cause of the Obstruction

Congenital Hydronephrosis.—The prognosis of congenital hydronephrosis is not good. The dilatation is often bilateral; it is secondary to ureteral obstruction. In some cases the obstruction cannot be found; the child comes into the world with large dilated kidneys, or these gradually increase in size after birth. There are cases of unilateral congenital hydronephrosis. The congenital defect is often coincident with other anomalies, including cleft palate, visceral abnormalities or other unique developmental faults—such combinations lead to early death. When the congenital obstruction is in the urethra, the dilatation of the pelvis and ureters may be (relatively) enormous. In other cases there is anomalous implantation of one or both ureters into the bladder, or the ureter may be placed at an abnormal angle, the ureter may be twisted on its own axis, there may be abnormal obliquity, the ureter may be completely occluded, converted into a fibrous strand. Anomalous distribution of the renal vessels has been observed in some cases. It is possible for hydronephrosis to be present at birth and of considerable size, secondary to congenital stone in the pelvis or ureter. Among some of the other anomalies are double ureters and double pelves on each side. In these cases the kidney substance is atrophied and there is simply a sac left holding the retained fluid.

Acquired Hydronephrosis.—Acquired hydronephrosis may be secondary to one of many causes. Morris in his original work on the "Surgical Diseases of the Kidney" reports 142 cases of marked hydronephroses in his 2,612 post mortem examinations.

Cancer of the pelvic organs, uterus, vagina, bladder or rectum was the leading cause of the obstruction, including 116 cases of the entire 142. This is an unusually large percentage and hardly corresponds with the experience of other observers.

Malignancy of the primary obstruction usually bars operation and makes relief impossible. The majority of my cases were due to calculi caught either in the pelvis of the kidney or in the ureter, low down, often

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looking into the bladder. Tuberculous ulceration and thickening of the renal pelvis or ureter, compression of the ureter by benign or malignant abdominal growths, ovarian cyst, rectal cancer, cancer of the prostate or bladder and the pregnant uterus are among the causes in my material.

Aschoff also calls attention to torsion of the ureter due to dislocation of the kidney. Stricture of the urethra, chronic cystitis with unrelieved residual urine during long periods have been observed by urologists. Following acute and chronic peritonitis, occasionally after major abdominal operations, adhesions, bands of new connective tissue and consecutive continuous obstruction lead to hydronephrosis. I have seen two such cases in which the relief of tension overcame hydronephrosis.

Cases have been reported by reliable observers (one quoted by Morris) in which the symptoms and characteristic urine of diabetes insipidus persisted with obstruction and hydronephrosis.

Kelly and Burnham make the statement after considering most of the possible causes of hydronephrosis that "abnormal movability of the kidney is undoubtedly the commonest single cause of hydronephrosis," and they claim that the successful results of fixation of such kidneys is proof of their contentions. "It is not, however, movability alone, but an associated condition such as that afforded by bands, blood vessels and adhesions, which terminate the formation of the pathological distention" (Kelly and Burnham).

(2) Whether the Lesion is Unilateral or Bilateral

Bilateral hydronephrosis usually offers a more serious forecast than does the unilateral disease. Obstruction below the pelvis is most likely to cause bilateral hydronephrosis. The *dangers of infection, atrophy* and *uremia,* are greater than with unilateral obstruction. *Stone in* both pelves or in both ureters low down, as in one of my cases may after years, with but few symptoms, suddenly cause *complete anuria* (in a man over 80 years of age) and death from uremia in less than one week. Considerably over 50 per cent of all cases are bilateral.

Of 665 cases collected by Newman, 227 were unilateral and 448 bilateral.

The *cause of death* with bilateral hydronephrosis is usually loss of renal function because of the atrophy, i. e., displacement by pressure of the kidney tissue. Some cases are enormously tolerant and the atrophy increases gradually; but in the end the fate of all is the same—uremia—unless death results from intercurrent disease. When bilateral hydronephrosis is due to obstruction which is operable, the dilatation is not abnormally large and the destruction of the renal parenchyma is not too far advanced (renal sufficiency fair) the prognosis for life is good.

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(3) If Unilateral, the Condition of the Second Kidney is of Paramount Importance

Life may be indefinitely prolonged in spite of unilateral hydronephrosis, so far as the kidneys are concerned, if the second kidney continues to functionate sufficiently. With organic disease of the second kidney—nephritis, nephrolithiasis, pyelitis—or other anomalies the prognosis is clouded.

(4) The General Condition of the Patient and Complications

The general condition of the patient is important. With acquired hydronephrosis, heart lesions, arteriosclerosis, syphilis, constitutional diseases or metabolic faults, as well as added serious infections or other medical and surgical complications, at once lower the chances of prolonging life for any length of time. *In old subjects with chronic hydronephrosis, intermittently emptying itself, even in the presence of advanced atheroma, the patient may continue to live in comfort but such a subject stands on the edge of a precipice all the time.*

Acute infection (pneumonia, influenza, typhoid or diphtheria) finds the subject with resistance far below normal and makes prognosis uncertain. Infection of the diseased kidney, causing pyelonephrosis, is always serious and can only be overcome by free drainage—ultimate nephrectomy. Such complication with the needed surgical interference is associated with a high mortality.

There are hydronephroses which gradually become purulent without marked constitutional disturbance during long periods.

In practice I do not recall a single case of *rupture of the hydronephrosis.* Such cases have been occasionally reported, and when operated at once offer a fair chance of recovery—when uncomplicated. Most of my patients who yielded to the hydronephrosis (usually bilateral) finally developed *uremia.* I have, however, had some unique and happy experiences with both unilateral and bilateral hydronephrosis due to stone with added uremic poisoning. One of my cases, a woman over 60 years of age, with double hydronephrosis after a severe double renal colic became profoundly uremic after a short period of shock. For over forty-eight hours there was complete anuria and coma. She made a happy recovery, so far as her uremia is concerned, and is now 68-70 years of age, comparatively comfortable. Such experiences are rare. In most cases of *anuria with uremia* death follows within a few days.

(5) The Time of Recognition and the Ability to Treat the Condition Surgically

Early recognition in cases dependent upon operable conditions adds enormously to the chances of success. Bilateral (congenital) hydronephrosis, in which the dilated pelves are palpable at birth or which increase

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rapidly after birth, offers a bad prognosis. There are successfully operated cases (nephrotomy) of congenital bilateral hydronephrosis on record but there are relatively few; surgeons have recommended plastic operations of this kind preparatory for more radical interference. In infants any kidney operation is serious, and unless the obstruction is easily operable success need not be expected. Congenital cases may offer no symptoms when the obstruction is slight or the hydronephrosis is small at birth and the condition under such circumstances is only discovered after much damage has resulted. Such cases are always serious.

Cases of hydronephrosis which are unilateral and which present to the surgeon early offer, because of improved methods of diagnosis (catheterization with cystoscopy, pyelography, sufficiency tests and cautious physical examination), a much better prognosis than ever before. It is only by these refinements of diagnosis that the condition can be detected early—and that means much for the patient and surgeon.

Advanced hydronephrosis is synonymous with destructive changes in kidney substance and a relatively bad prognosis for the restoration of the diseased kidney. With the second kidney as already suggested free, the prognosis for life is good in the absence of complications, including constitutional anomalies. Such cases in resistant subjects offer a good prognosis after radical surgical interference. With the second kidney involved or with ascending infection in one or both kidneys, particularly the latter, the results of surgical interference are discouraging. It is often surprising to find prompt response from the surgical operation of bilateral hydronephrosis though only a small remnant of kidney tissue remains.

Incising and draining the kidney sac (nephrostomy) leads to the establishing of a urinary fistula which usually discharges during a long time. In almost 50 per cent of these cases the sac finally collapses completely and the fistula closes. In the remaining cases the fistula persists; the patients live during varying periods—sometimes for years; they die of intercurrent disease or they become infected, emaciated, develop amyloid degeneration of several organs and die with the usual symptoms of amyloid kidney and liver (dropsies, anemia, etc.).

The percentage of successes with nephrectomy for unilateral hydronephrosis and a healthy second kidney is most encouraging. Cases of uncomplicated unilateral hydronephrosis due to stone in the pelvis of the kidney or ureter on the same side in which the obstruction was removed by the extraperitoneal method have given almost uniformly favorable results.

Conclusions

The prognosis of hydronephrosis will grow more favorable as time advances, for the modern methods of diagnosis, already mentioned, now

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practiced by urologists, will be more generally used in the future; technic will be improved and radical surgical treatment will not be postponed until life is threatened. In considering the prognosis of individual cases the *secondary bladder and ureteral changes* are not to be ignored.

The prognosis of hydronephrosis following malignant growths either within or without the urinary tract is almost uniformly bad. The late recognition of the primary cause makes the forecast ominous.

The surgical relief of *fibrous bands* or other *operable ureteral obstruction* offers an encouraging prognosis.

The great dangers are atrophy of kidney substance, final anuria and uremia, which may result from the unrelieved obstruction, also sepsis. It is possible for renal and ureteral obstruction to lead to moderate hydronephrosis; the sac may collapse; finally there is atrophy of the kidney.

Enormous dilatation may persist with intermittent discharge of the fluid (*intermittent hydronephrosis*), the patient living during many years. These cases are often operable and permit of successful plastic operations; they include sections of valves, ureteropyeloplasty, ureteropyeloneostomy, lateral ureteral anastomosis, plastic operations on the renal pelvis, pyeloplication, orthopedic resection and combined operations. Schloffer has reported 86 such operations, with 7 deaths and 17 failures. There are occasional cases in which the sac may discharge and the fluid may never reaccumulate. The conversion of a sterile hydronephrosis into a pyonephrosis is possible. These sacs often rupture externally or are surgically treated after they point. The rupture may take place in one of several directions (See Pyonephrosis and Pyelitis). Early surgical treatment offers great encouragement for these purulent accumulations.

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(*h*) *Nephrolithiasis*

(*Renal Calculus, Calculosis of the Kidney and Ureter, Nierenstein*)

Cause.—The deposition or precipitation of normal or abnormal solid constituents of the urine (often dependent upon marked diathesis) usually layer upon layer around a nucleus, is the cause of calculus formation which, as a rule, is held in the pelvis of the kidney or in the substance of

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that organ. Stone may be caught in the ureter—either a prolongation from a pelvic stone or the calculus may find its way down the tube to be caught—usually below the brim of the pelvis, most frequently near the bladder. Calculi may fall into the bladder and there by aggregation grow, or they may be passed per urethram. In rare cases the stone may fall into a diverticulum of the bladder, either remain there without causing serious mischief or, as often happens, it gradually increases in size ultimately becoming a formidable body in the bladder. Renal calculus may form in the substance of the kidney; several stones may plug the calices, or the kidney pelvis may hold one or more calculi during varying periods without materially influencing the health or comfort of the carrier.

Varieties of Calculi.—When there are only small rough or gritty bits, these are spoken of as *"sand"* or *"gravel"* and such particles are often passed without pain or constitutional disturbance. Millet-seed-sized gravel or even larger calculi are often passed unnoticed and without symptoms. The most frequent calculi are *uric acid* and *lime oxalate;* in the bladder with decomposing urine a calculus which is hard (oxalate or uric acid) may be surrounded by phosphatic deposit precipitated from the urine. The *reaction of the urine* is the prominent factor in determining the character of the precipitate. *Cystin* stones, also *xanthin,* are exceedingly rare (See Cystinuria). There are occasionally phosphate and carbonate of lime, also triple phosphate calculi. One or more stones may remain in the pelvis of the kidney without symptoms when suddenly there is a renal colic in which the pain and other accompanying symptoms are characteristic. The stone or a part of it may find its way into the bladder; it may remain unmoved; it may become caught in the ureter, or what rarely happens, it may, because of its size or other anomalies, wander from the urinary tract after perforation at some point either into the perinephric tissue (See Perinephritic Abscess), into the peritoneal cavity or into one of the surrounding organs.

Prognostic Features

Single calculi without infection offer a good prognosis. In about 50 per cent of all cases there is but one stone. *Multiple calculi* are frequent. Israel says that both kidneys are involved in 27 per cent of his cases of renal calculosis, while Lequen claims 50 per cent; Hugh Young holds that these figures are too high. The size and shape vary. *Casts of the pelvis* in coral-shaped and large stones are not unusual. In some of these cases the pelvis is tightly drawn over the stone, in others, when infected, the concretion lies in pus. *Large calculi* with septic symptoms are unfavorable.

The x-ray has opened an important diagnostic field for the prompt and certain localization of calculi within the urinary tract; the x-ray shows calculi most distinctly which cast the deepest shadow. In order

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of their density therefore, the denser calcium oxalate shows best, then the phosphatic, and finally uric acid stones (gall-stones are less likely to show than are renal calculi).

With ureteral stones it is wise to make repeated plates, and it should be remembered that if caught they are found below the brim of the pelvis at the junction of the ureter and bladder. The recognition of renal and ureteral calculi early by means of the röntgenogram has enormously improved the prognosis of ureteral and renal calculosis, for it leads to early radical treatment and therefore prevention of infection and secondary local changes which must of necessity follow from the presence of the foreign body. The prognosis of those cases in which one or more calculi are held in the kidney, without causing more than a mild grade of pyelitis (See Pyelitis) is good, as a rule. These patients may live without any symptoms, and the presence of a pyelitis calculosas is only recognized by an examination of the urine, usually for life insurance; the stone is detected by x-ray examination or it may suddenly provoke renal colic, or without marked symptoms it falls into the ureter. If the clinician subjected his clients who show evidences of pyelitis or obstruction to x-ray examination he would very often detect renal stone in its incipiency or at a time when the secondary changes have not advanced or infection, the greatest danger, has not occurred. A single plate which may prove negative is insufficient for diagnosis; a single positive picture is convincing and cannot be controverted.

Stone in the ureter, usually below the brim of the pelvis (Tousey), if held for any length of time may lead to secondary changes, dilatation, hydronephrosis, infection (pyelonephrosis and septic fever). In these cases the prognosis must always depend upon the ability to overcome secondary changes by removing the cause, also upon the resistance of the patient (See Pyelonephrosis).

Stone in the pelvis of the kidney may cause no pain, but yet pyelitis may be sufficient to cause constitutional symptoms and materially reduce the patient during long periods. Here urine analysis and x-ray must aid in diagnosis and suggest treatment. In pregnant women I have diagnosticated cases of previously unrecognized renal calculosis during Bacillus coli infection by x-ray examination. At times such complications may threaten life; the fetus may be prematurely expelled, after which the condition may become latent. The presence of the stone is almost forgotten until renal colic proves a sufficient reminder and the case is usually treated successfully by surgical means.

A large stone in the pelvis of the kidney may not always cause marked subjective symptoms; urinary examination, cystoscopy and ureteral catheterization and examination of the segregated urine will, however, prove advancing encroachment on the parenchyma of the organ, and in most cases pyogenic infection follows. Such cases, when the second kidney

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is not infected or diseased and there are no other complications of moment, offer a favorable forecast following the surgical treatment most indicated.

It occasionally happens that a patient dies suddenly during a *renal colic.* Such subjects are usually arteriosclerotic, have myocardial insufficiency, or they suffer from some form of nephritis. The *shock of renal colic* does occasionally lead to anuria (calculous anuria), and uremia may develop. I have seen cases, in which after double renal colic and the passage of calculi, anuria and uremia persisted between two and three days in patients advanced in years, which finally recovered.

It may be safely assumed that in patients with marked *diatheses, hereditary tendency* (several members of the same family often suffer from metabolic faults—diabetes, gout, cholelithiasis) and *renal lithiasis* at the same time, the prognosis is not encouraging, for with all of the above mentioned anomalies there is very often *cardiovascular* (arteriosclerosis) *disease,* in some cases marked *tendency to obesity.*

The majority of patients who during or after renal colic pass the offender, in whom, after such passage the urine appears normal during from six to nine months, in whom there is no remnant of symptoms either objective (x-ray) or subjective, rarely have recurrence. This has been my experience based upon many years of observation; with strong *hereditary tendencies* the rule may need modification. I have rarely seen recurrence after the passage of a calculus of congenital origin.

Calculi in both pelves are always a menace. Sudden complete anuria may cause overwhelming and fatal uremia (See Uremia). *When renal calculi lead to suppuration the only hope of complete cure lies in prompt surgical interference.*

Renal or ureteral stone with nephritis, heart lesions, advanced arteriosclerosis, constitutional or metabolic disease offers an unfavorable prognosis for life. While neglected nephrolithiasis is most likely to become infected, it not infrequently happens that sclerotic (interstitial) changes are produced in the kidney holding the stone, and *secondary heart and arterial changes result.* The pain of nephrolithiasis other than the renal colic is usually in the back, is often constant and nagging on the affected side but does not materially interfere with the activities of the patient. The *hematuria* is less profuse than with cancer or tuberculosis and in my experience has never threatened life.

The *temperature* may be elevated, the *nausea* and *vomiting* exceedingly troublesome and weakening, the *pulse* often rapid during the attack (renal colic) but unless there are associated conditions the patient rallies in a few days. It not infrequently happens that with one or more small stones, renal colic—severe and exhausting—recurs at short intervals; sometimes there are several seizures during a single day. In most of these the stone passes per urethram without being held after it enters the bladder.

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The prognosis of *pyelitis calculosa* has been separately considered (see Pyelitis); when there is added infection (purulent) as repeatedly suggested, *intermittent fever* persists until radical treatment removes the focus. *Blood counts* showing marked *leukocytosis* in these cases offer valuable diagnostic and prognostic data coupled with *x-ray* pictures and *pyelography.*

Persistent pyuria with or without renal colic which cannot be explained in any other way, particularly if the patients are of full habit, should make the clinician suspicious of renal calculus.

An *acid urine, pyuria (moderate), kite-shaped epithelia, shingle arrangement of the epithelia are characteristic of pyelitis; when with this picture we also find uneven crystals with irregular and ragged prolongations, the diagnosis of pyelitis calculosa is justified and the prognosis should be framed accordingly.*

The surgical treatment of *calculous anuria* is unfavorable. The *period of tolerance* is often surprising and has justified procrastination. The cautious study of cases in which the obstruction is one-sided, with calculous anuria resulting in spite of the surprising tolerance, leads to the conclusion that the safest time to operate is before uremia supervenes—for the mortality increases with each day. Huck found that before the fourth day the mortality is 25 per cent, before the fifth 30.7 per cent, and before the sixth 42.1 per cent (Walker). Watson (quoted by Walker) collected 205 cases of calculous anuria and reports:

> "Treated without operation, 110; deaths 80; mortality 72.7 per cent.
> Treated by operation 95; deaths 44; mortality 46.3 per cent."

Walker adds: "These results are capable of improvement if the necessity for early and rapid operation is fully realized."

The mortality following operations for stone (nephrolithotomy) in healthy or slightly infected kidneys and in *infected kidneys,* as shown by collective investigation, is 8.8 per cent for the former and 23 per cent for the latter (Legueu). *It may be concluded that the carrier of a stone in the kidney or ureter is not a safe risk; he is constantly in the midst of more or less danger though spontaneous cure is not impossible nor unusual. The dangers are infection, prolonged anuria, possible uremia, perforation into the peritoneal cavity, occasionally erosion of the renal artery, pyelonephrosis and cystitis (ascending infection), final sepsis, amyloid degeneration and paranephritic abscess, hydronephrosis and interstitial nephritis* (Luthje).

For further data relating to the prognosis (surgical) of renal and ureteral calculosis, the reader is referred to the well-known works of Israel, Henry Morris, Küster, Kelly and Burnham, Guiteras, Rovsing, Keen and Harrison. (See Index Medicus and Index Catalogue—Surgeon General's Office.)

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(i) *Neoplasm of the Kidney (including Hypernephroma)*

General Statements.—Renal growths may be primary or secondary, benign or malignant. They are not frequent, are difficult of recognition unless they produce symptoms, or are palpable. They are often palpable before they cause symptoms sufficient to bring the patient to the physician, because of the tolerance of the organ invaded and in many cases the slow growth. In some the superimposed panniculus is sufficient to make early recognition exceptional.

Malignant Growths

The majority of malignant growths of the kidney (carcinoma) are secondary. Morris in 2,610 post mortem examinations (of kidney diseases) found 5 primary and 22 secondary cases of malignant disease of the kidney. Rolleston found but one primary renal growth in six and one-half years at St. George's Hospital; in 10 years 5 cases were met in the pathological department (Kellynack).

At Würzburg Virchow found only 0.5 per cent of the malignant neoplasms involving the kidney. Kellynack reports among 1,400 cases of kidney lesions while he was pathologist in the Manchester Royal Infirmary, 6 cases of primary renal growth.

Sarcoma—Carcinoma.—In my experience sarcoma of the kidney is more common than carcinoma; many cases reported as cancer are unquestionably sarcoma. The more frequent seat of the primary cancer is the alimentary canal. Kellynack says "that secondary deposits are met with in the kidney in about 8 per cent of all cases of cancer and nearly 14½ per cent of all cases of sarcoma."

It is the consensus of opinion among pathologists and clinicians that

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the kidney is comparatively seldom involved in secondary growths and that primary growths are exceedingly rare.

Congenital sarcoma is not uncommon; if small it may escape notice; it often grows to enormous size before it is detected—too late for an encouraging forecast in most cases. It may be of enormous size at birth, a smooth globular mass filling the abdomen.

My experience with sarcoma in children has been unfortunate; operated on detection, they have recurred within less than twelve months in most cases in spite of what appeared to be a radical operation.

Hypernephroma.—Grawitz in 1883 called attention to a growth since known as *hypernephroma.* The growth arises from *"aberrant renal rests."* My observation of the material of Fischer, in Frankfurt on the Main, during almost an entire year convinced me that most renal growths were true hypernephromata and that in most of these the recognition of the disease was too late to anticipate metastases. In my experience the metastases to distant organs are comparatively early; in the most favorable cases recurrences or fatal metastases are not long postponed; in the more favorable cases after comparatively early operations, with but few exceptions, there are positive evidences of return or metastasis within between two and three years. The metastases have frequently been to the spine and brain, in one case to the heart, to the lung in a number of cases, and to the bones of the extremities. There are but few cases on record with the diagnosis positively established in which hypernephroma, unless operated very early, offered hope of permanent cure. Israel reports 2 cases alive after two years, 2 after six years and one after nine years.

Prognosis of Malignant Diseases of the Kidney.—With the data before us concerning sarcoma and carcinoma, the fact that so many of these kidney tumors are secondary, that they are long tolerated, that the kidney mass is often a part of a general carcinomatosis or sarcomatosis, that most operations are late—the prognosis of both must be exceedingly grave. My cases secondary to growths in the testicle have been rapidly fatal, often with liver metastases at the same time.

Renal tumors (malignant) may remain latent or increase insidiously over a very long time, the general condition may not be materially affected during many months; *hemorrhage,* a leading symptom may cease and lull patients into a false and unjustified feeling of security. The growth may be palpable during long periods before there is retrogression.

With *papilloma of the kidney,* hematuria may be paroxysmal during many years (in one of my cases over twenty years) before there is progression to a fatal termination. In the case above mentioned the bladder and kidney were both finally involved and there were metastases to distant parts.

The entire consideration of the prognosis of the malignant diseases of the kidney may be summarized in a short paragraph: *"All malignant*

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growths of the kidney are surgical affections in which the only hope of permanent relief lies in the early recognition of the growth when it is primary and its prompt and radical removal. Secondary growths, which are numerically in the ascendency offer no hope of permanent relief by any means at our command at the present time."

The benign growths of the kidney include the fibroma, lipoma, angioma, lymphadenoma and myxoma. They are exceedingly rare, may cause no symptoms or but few, and offer a good prognosis. The majority of benign growths are discovered on the post mortem table.

The reader is referred to the authoritative surgical treatises mentioned at the end of the preceding chapter for fuller information on this subject than I am able to give in a medical work.

Cysts of the Kidney.—With chronic nephritis, tubal and parenchymatous, cysts of varying size are often found; they are usually small, due to dilatation of constricted tubules. They are not of sufficient size to be palpated and are not recognized *intra vitam*—are not of great prognostic significance.

Polycystic Kidney.—Polycystic kidney is an interesting condition from the diagnostic and pathologic standpoint, but it is not amenable to cure though there are recorded cases in which death has been postponed during several years. The condition may continue during many years; indeed with recurring characteristic symptoms patients may live to reach old age. The majority die between 40 and 60; of these the death rate between 40 and 50 is highest.

The *leading symptoms* are paroxysmal hematuria and pain which recur at long or short intervals during many years with physical signs of a renal mass; in thin subjects its contour leaves little room for doubt in diagnosis. The size of the cyst varies—several may be small while in the same kidney one or two or more cysts are of considerable size. The lobulated appearance of the kidney is often recognized through the abdominal wall. The condition is almost always bilateral, though French observers have concluded from the study of a large material that almost one-fifth are unilateral.

Morris' statistics are quoted by those who favor surgical interference as encouraging. At best they cannot avert the fatal termination, for these patients die with symptoms of chronic nephritis, characteristic cardiovascular changes and uremia. The urinary features include the low specific gravity, hyaline and granular casts and other features of interstitial or secondary contracted kidney.

Osler has recently reported two interesting cases of *polycystic kidney* in the adult recognized *intra vitam*—one died while under observation, the post mortem confirmed the diagnosis. Whatever surgical operation is performed, the mortality is high and it is questionable whether life is materially prolonged where there are bilateral cysts. With *unilateral*

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polycystic kidney surgery offers greater hope—but a high mortality. There is a strong hereditary character; several members of the same family may be afflicted.

When the cysts are large at birth, life is not prolonged and associated congenital anomalies are common.

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(*j*) *Movable Kidney*

(*Mobile Kidney, Nephroptosis, Floating Kidney, Renmobilis*)

This subject has been fully considered from the medical standpoint in Section V, F. 4, gastroptosis, also enteroptosis (Glenard's disease in same section).

Operation.—The operation of kidney fixation is less frequently performed than it was ten or fifteen years ago. Failures have been repeated and in many the subjective complaints have persisted after the operation.

Mortality Following Operation.—The mortality following the operation is between one and two per cent. I have considered the results obtained by Treves in Section V, to which reference is made above. In America, Edebohls collected 846 cases from the literature, with a mortality of 1.65 per cent. Billington operated on 575 patients with 4 deaths.

Short says: "Probably the mortality is between 1 and 2 per cent." For detailed surgical statistics the reader is referred to the works of Billington, Morris, Rovsing, Keen, Mills of Birmingham, the reports of the London Hospitals, Bristol Hospitals, the Mayo Clinic, Kelly and Burnham and Guiteras (See Index Medicus). Statistics which are intended to prove the curability of the condition by operation are unreliable. Most patients with movable kidneys are neurasthenics and in many the mobility of the organ is only a part of a process which includes many organs (Glenard's disease).

Associated Symptoms.—Cases in which there are repeated *Dietl's*

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crises, which are not relieved by mechanical support, in which there is repeated kinking of the pedicle, demand surgical interference. In my experience the crises were overcome by radical treatment, but many, indeed most of the neurasthenic symptoms persisted.

Cases with hydronephrosis have given disappointing results; this is particularly true of intermittent hydronephrosis unless some radical measure was instituted to prevent kinking of the ureter because of the mobility of the kidney.

The association of *gastric ulcer* with movable kidney is surprisingly frequent.

Prognostic Factors.—The *autosuggestion* practiced by the subjects of this condition is overpowering and with many mental symptoms is often, but not always, relieved by surgical treatment. I have found over 50 per cent of nervous patients in private practice and a large percentage in dispensary material the subjects of movable kidney.

In my experience the regulation of the habits of the patient, well-timed and repeated suggestion, proper mechanical support and healthful occupation are more important and offer better results than does radical surgical treatment. Organic diseases of the stomach and intestines have often been suspected, when mobile kidney alone was responsible for such simulation. In some of these cases it requires the most cautious and long-continued personal supervision before positive differentiation is possible. In a small proportion of these cases *the effect of surgical interference* proves wholesome *per se* though failures are not unusual.

In offering the prognosis in the average case of movable kidney with neurasthenic accompaniment the diagnostic ability, tact and discriminating sense of the attendant are all taxed and upon his judgment and personality the future welfare of the patient often depends. I have seen many cases in which the strong personality of the attendant has been sufficient with mechanical support to make the patient comfortable and keep her so.

Suppurative Diseases of the Kidney

(*k*) *Pyelitis*

(*Pyelonephritis, Perinephritic Abscess, Nephritic Abscess, Suppurative Nephritis, Pyonephrosis*)

General Statements.—While the preceding terms are generally considered to be synonymous, they are not really so. *Pyelitis* is literally an inflammation of the renal pelvis; *pyelonephritis* includes pyelitis and nephritis; *perinephritic abscess* is a pus accumulation about the kidney (in the perinephric tissue); *nephritic abscess* and *suppurative nephritis* are synonymous with abscess of the kidney. *Pyonephrosis* includes the break-

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down of the parenchyma of the kidney substance (atrophy) in a process of suppuration. The organ is practically converted into a pus sac.

Pyelitis as well as (e) perinephric abscess (g), hydronephrosis (h), nephrolithiasis (i), neoplasms of the kidney (including hypernephroma), and (j), mobile kidney—the conditions included in 2 of this Section VI—are all surgical affections which as a rule find their way to the internist for diagnosis, and I therefore feel justified in considering their prognosis without entering into the detail which has been given to the strictly medical diseases included in this section (See also Section VI—Anomalies of Urinary Secretion— (c) *Hematuria* for the consideration of *Acute and Chronic Primary Infections, non-calculous pyelitis with moderate hematuria,* usually found in pregnant women and at the menstrual period due to the Bacillus coli communis as a rule, though occasionally other pathogenic bacteria may be the cause. About 30 per cent of these cases abort. This condition is also known as *pyelocystitis*).

Prognostic Factors.—*Pyelocystitis* may be *acute* or *chronic.* When the urinary tract has been normal the infection is usually ascending, oftener of Bacillus coli origin than of any other infection and secondary to some intestinal disturbance including appendicitis, colitis (acute or chronic), proctitis, hemorrhoids, dysentery or other grave intestinal disease (carcinoma, ulcer, etc.). With the benign infections and pyelitis the course of the disease is favorable. In old men with intestinal lesions and consecutive pyelitis (pyelocystitis) septic symptoms may be prominent early and overpowering. Such subjects soon become thoroughly toxic, the kidney is tender, at times palpable and enlarged, and the prognosis is bad.

When the symptoms are profoundly toxic, there may be repeated chills, high fever and rapid pulse. The prognosis depends upon the ability of the patient to offer sufficient resistance during the acute period to withstand the added infection. The course of the disease in old and enfeebled subjects is rarely more than seven to ten days when toxemia is deep. The infections, as already stated in considering the prognosis of cases in pregnant women—to which we also refer above—is favorable in most cases. The condition in our experience has improved with the emptying of the uterus.

Pyelitis in enfeebled subjects due to exposure to cold and wet with added infection is often associated with symptoms of grave constitutional disturbance, and may lead to abscess formation or a deep toxic condition from which the patient does not rally. The majority of pyelitides, in which the etiology is obscure, in patients with normal or even slightly reduced resistance, recover.

Catarrhal pyelitis may become chronic when due to stricture of the urethra, cystitis, stone in the bladder, ureter or pelvis of the kidney, tuberculous disease of the organ or the urinary tract below the pelvis.

With tuberculosis of the genito-urinary tract there may be suppuration

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due to the degeneration of the tubercle and breakdown of included tissue in both the pelvis and kidney substance at the same time (See Tuberculosis of the Kidney—Section I).

Surgical Interference, etc.—Pyelitis, upon whatever cause it depends, if unrelieved, is likely to encroach upon renal tissue causing breakdown and suppuration. When pyelitis is secondary to kidney infection, the disease beginning in the substance of the organ with abscess formation, surgical interference offers the only hope of saving the organ, or nephrectomy offers the only hope of saving life once the disease is far advanced.

It is plain that the prognosis of pyelitis must often depend upon the ability of the surgeon to remove the primary cause, the extent of coexisting lesions, the resistance of the patient and the depth of the toxemia. The condition of the second kidney is of paramount importance and the examination of the segregated urine with the assistance of the ureteral catheter and the cystoscope and its thorough study both chemically and bacteriologically, beside x-ray pictures, will always supply data of great prognostic value which demand expert and cautious interpretation.

With *acute pyelonephritis* the English have not had encouraging results from nephrotomy. Walker reports 7 deaths among 20 operations (35 per cent). He says: "In surviving cases, the late results are also unsatisfactory; the acute symptoms subside, but chronic pyelonephritis persists, and nephrectomy may be required later."

In America the results of nephrectomy in pyelonephritis have been most encouraging in the presence of a healthy second kidney. Almost all of these cases, when uncomplicated, recover. Walker reports 17 nephrectomies without a death for pyelonephritis.

Symptoms of chronic cystitis with all forms of chronic pyelitis are persistent and never yield until the renal lesion has been successfully relieved.

Catarrhal pyelitis is likely to recur after supposed relief. In all of these cases stone in the pelvis of the kidney should be strongly suspected. The x-ray will prove a valuable adjunct, not only for diagnosis but for prognosis as well.

Calculous pyelitis may cause symptoms of acute pyelitis during a limited period; the urine may practically clear and the patient as well as the attendant are deluded to believe that complete cure has resulted. Unless the stone is passed or in some way encysted—which is comparatively rare—the colic with hematuria recurs with other urinary and x-ray evidences which prove the presence of the offender (See Nephrolithiasis). The prognosis of these cases is good in resistant subjects who are without serious complications.

One of the leading dangers of neglected pyelitis calculosa is ascending suppurative nephritis with consecutive renal insufficiency and uremia (See also Nephrolithiasis).

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Ascending pyelitis from an infected prostate may be either acute or chronic. Most of these cases are chronic and yield only to the radical treatment of the primary disease.

Gonorrheal pyelitis in spite of rigorous local treatment is exceedingly rebellious, and complete cure is exceptional though patients live for years unless there are complications, including (occasionally) gonococcus endocarditis—always fatal.

Neglected pus accumulation in the pelvis or kidney usually finds exit in one of several directions. It may lead to *perinephric abscess* or it may *perforate into the free peritoneal cavity causing peritonitis and death.*

When the pus is encapsuled or there is a sinus which continues to discharge and the diseased kidney is not removed, the patient usually dies after months of suppuration and often amyloid disease in many vital organs (liver, spleen and kidney). I cannot accent with too great force the assistance in prognosis which may be received from the CORRECT INTERPRETATION OF CYSTOSCOPIC EXAMINATION WITH URETERAL CATHETERIZATION, PYELOGRAPHY, X-RAY EXAMINATION, CHEMICAL AND BACTERIOLOGICAL METHODS AND BLOOD EXAMINATIONS.

Most cases of pyelitis which to all appearances make full recoveries are not *bacteriologically cured,* for according to Scheidemandel, only 35 per cent of acute cases which are relieved of subjective symptoms in from five to six weeks are found with sterile urine. 30 per cent of the remaining cases fall into a chronic latent period which may persist during many years without advance of renal lesions.

Acute pyelitis occasionally attacks babes during the first months of their existence, when it is likely to be due to the Bacillus coli communis. Most of these babes recover after an acute and threatening period in which there is high fever with evidences of profound toxemia, at times convulsions. Older children may also become infected. The average duration of these forms of pyelitis in children is from seven to ten days.

Chronic pyelitis is frequent in the urological clinics. Of 1,800 urological cases Fritz found 161 cases without involvement of the parenchyma of the kidney. Of these 56 were males, and 105 females. The right side was involved in 87, the left in 32 and both sides in 42 cases—the right side therefore in 129 and the left in 74.

Chronic pyelitis may exist during years without encroaching on the parenchyma of the kidney. The treatment of such cases, purely local (pelvic lavage), has in properly selected cases proved eminently successful (Geraghty). The uncomplicated cases of pyelitis are without reduction of kidney function; pyelonephritis when advanced always shows decreased function.

Geraghty contends that the organism causing infection has very little influence on prognosis. *Pyelography* is of considerable prognostic value, for it shows the condition of the pelvis resulting from the infection.

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The prognosis after local treatment of the pelvis is particularly good in cases of "fairly active infection with a normal function and in which the collargol shows few changes in the pelvic outline."

In the chronic cases, i. e., "long standing pelvic infections, in which marked changes have occurred in the pelvic wall, as shown by pyelography, and in which one finds in the catheterized specimen very few lekocytes and only an occasional bacterium, the prognosis is not so favorable." When with chronic pyelitis there is marked dilatation of the renal pelvis, residual urine and bacteriuria, the prognosis for restoration of the kidney is bad.

Some of these chronic cases may develop renal calculosis or finally pyonephrosis (Lenhartz).

Of 80 cases reported by Lenhartz, to whom we owe much of our knowledge concerning pyelitis, there were 5 deaths—one due to cancer, one tuberculosis, two pyonephrosis and one ended after acute and severe symptoms of pyelitis with renal abscess due to the Friedlander bacillus.

Suppurative nephritis or abscess of the kidney is a suppurative inflammation of the kidney substance dependent either on hematogenous or lymphogenous origin, to direct or indirect infection from traumatism or extension by contiguity from suppurating neighboring organs. The disease, when not part of a general pyemia, may be one-sided, but it is unually bilateral. When there is obstruction of one ureter or the suppuration spreads from the pelvis of the kidney, the abscess is likely to be unilateral. With fully developed suppurative nephritis the destructive process includes all of the renal structures and the abscess may be single or multiple. Multiple abscesses of the kidney may become confluent because of the destruction of intervening tissue and *pyonephrosis* (pyelitis with suppurative nephritis and atrophy of the kidney substance) results. The organ becomes a pus sac. With all forms of suppurative diseases of the kidney the symptoms, objective and subjective, are outspoken and usually make a reasonably positive forecast possible. With pyonephrosis Brown quotes Küsler as offering "four favorable factors in the prognosis—the possibility of an early correction of the urinary stasis, youth, a strong constitution, and a unilateral lesion."

The urine always shows pus in varying quantity. With pocketing it may be intermittent, a large discharge may be unloaded but once daily, usually on arising in the morning. If the ureter is constricted there may be but little pus during part of the day and a free discharge at one time, or the *pyuria* may recur at longer intervals. Renal casts are not infrequently found. With simple catarrhal pyelitis kite-shaped epithelia shingle-arranged with a few pus cells and moderate albuminuria are characteristic. The urine is usually acid but not necessarily so; the reaction depends upon a variety of causes and on the responsible micro-organism. Urine with shreds of renal tissue, with the appearances mentioned, proves

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advancing destruction of renal tissue; unless relieved surgically, the outcome is fatal.

Repeated chills and fever are indicative of progression and toxemia. I have learned to recognize these symptoms with tuberculous nephritis and pyelonephritis as indicating invasion which can only be relieved by radical surgical means. *With both tuberculous and pyemic conditions, if the patient lives long enough, progressive anemia is finally associated with amyloid degeneration and death.*

In some chronic cases after a few days of chills and fever, there is a free discharge of pus and a return to a fairly comfortable condition during a long period. Recurrence of symptoms is the rule. Finally the chills and fever and pyuria become almost continuous; the fever is characteristic of pyemia; the pulse grows more and more rapid, and with symptoms of profound invasion of the nervous system these patients die (coma, etc.). It is often surprising to find on post mortem examination the presence of pyonephrosis, tuberculous or non-tuberculous, in subjects who have never complained of renal symptoms and in whom the development of acute symptoms, often suggestive of uremia or overwhelming toxemia (non-uremic), end life within a few hours or days.

Pus in the kidney may become encapsuled, may pass through the ureter, may burrow and find a safe exit—all without destroying life. Nature's reparative and conservative processes occasionally come to the rescue, but the majority of cases must be saved by modern surgical methods. Permanent damage to the kidney with all forms of suppurative disease of that organ is best prevented by the full appreciation of the old surgical principle that pus accumulation is best treated by free drainage.

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(*l*) *Perinephric Abscess*

(*Perinephritis, Epinephritis, Paranephritis, Paranephritic Abscess*)

General Statements.—Brown, whose consideration of the suppurative diseases of the kidney is truly classical, in considering the nomenclature, says: "It is better to be more explicit, however, and to define *perinephritis*

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as inflammation of the fibrous capsule immediately surrounding the kidney, *epinephritis,* inflammation of the fatty capsule, and *paranephritis,* inflammation of the retroperitoneal fat." The differentiation *intra vitam* is exceedingly difficult, unlikely, and for all practical purposes, unnecessary.

Origin.—Most perinephritic abscesses are unilateral, acute, and when developed the pus is collected around the kidney in the lumbar region. My experience agrees with that of Guiteras which he expressed ten years ago that nearly all cases of perinephritic abscess are due to kidney disease and "that those secondary to diseases of other organs are rare and not, properly speaking, perinephritic abscesses." He found that 85 per cent of perinephritic abscesses were due to kidney disturbances; these he classified as follows, reporting 20 cases:

Pyonephrosis:	
Calculous	3
Tuberculous	5
Obstructive	3
Total	11
Pyelonephritis:	
Calculous	1
Tuberculous	2
Obstructive	2
Total	5
Rupture of kidney	1
Empyema	1
Necrosis of rib	1
Unknown cause (probably retroperitoneal gland suppurating)	1
Total	4
Full Total	20

Prognostic Factors.—In my experience I have no death to record resulting from perinephritic abscess *per se* when the complication was recognized reasonably early and the abscess was freely drained. Cases not recognized, but neglected, have died of pyemia perforation (peritonitis) or from other causes. The prognosis of perinephritic pus accumulation rests largely upon the *nature of the primary kidney lesion and timely recognition.*

When there is primary pyelonephritis or pyonephrosis with paranephric suppuration, unless the primary abscess cavity is removed the chances are against full recovery, and one or more sinuses usually remain with annoying urine discharge. In unrecognized cases there may be burrowing,

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depending upon the position of the abscess, the point of least resistance and the extent of the complications (adhesions, etc.).

Perforation may be either visceral or ventral. Perforation or pointing in the lumbar region (ventral) is more favorable than rupture into the peritoneum, intestines, stomach or pleural cavity (visceral). In a fair number of cases *fistulae in the lumbar or inguinal regions* persist during considerable periods, and finally heal spontaneously. When the renal suppuration leads to sepsis (acute and malignant) the organ breaks down rapidly, the sloughs show a gangrenous process, and the patient dies with symptoms of profound toxemia *unless saved by timely surgical interference.* Rosenberger's statistics show 26 cases of perforation—6 were into the intestine, of these 2 died; 13 into the pleural cavity, with 8 deaths; 3 into the free peritoneum, with 3 deaths. Early recognition, with *prompt drainage* overcomes the danger of the complication; the surgeon then has the primary lesion to combat.

There are a number of cases in which pus accumulation is found about a kidney without evidence of any underlying renal lesion—so-called *"primary cases";* these when recognized early, pointing outward, offer a good prognosis. When drained by surgical means they recover promptly. I have met a few cases in which perinephric abscess followed typhoid fever and pneumonia; in these recovery was complete.

Perinephric abscess does not often present for diagnosis in the practice of the internist. In private practice I have seen but 5 cases among my last 6,600 cases. In hospital practice I occasionally find a case to be transferred to the surgical side. At the Johns Hopkins Hospital among the white *surgical* patients during the period from 1892 to 1911—18,448 males and 6,934 females—there were 18 cases of perinephritic abscesses, all among the males, with 2 deaths (11.1 per cent). There were no cases among the females. We note that the statistician Hoffman includes 6 cases of perinephritic abscess in his "white *medical* cases"—all in males, and without a death.

Küster reports 230 cases of paranephritis, of which 145 made a complete recovery; in 6 there were fistulae, 79 died (mortality 34 per cent). These cases prove *neglect of early diagnosis or treatment,* for it is not in accord with the experiences of the clinician at the present time, either in our own country or in Europe.

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Section VII

Diseases of the Nervous System

A. Diseases of the Peripheral Nerves

I. Neuralgia

General Considerations.—Neuralgia is a *symptom, it is never a disease per se*—a fact which must be kept before the mental vision of the clinician for all purposes of diagnosis, prognosis, and treatment. That there are many acutely arising paroxysmal pains which course along one or more single nerves or nerve trunks in which the true pathology escapes detection, which yield to treatment, must be admitted.

Those "neuralgias" are dependent upon *nerve pressure, perineuritis oftener than neuritis, true structural irritative disease of the nerve, or upon change of a nutritional character in which no structural change in the nerve can be demonstrated.*

The word "neuralgia" is carelessly used by the physician very often, and should be limited to the *idiopathic* nerve pains in which it may be assumed after thorough consideration of the individual case, that there is no pathologic change.

The classification of Herter should be accepted which divides all neuralgias into either *"idiopathic,"* those without evident lesion, and *"symptomatic,"* those depending on structural disease, usually neuritis or perineuritis.

Definition.—Neuralgia may be defined as a pain, arising suddenly, without prodomata, of a shooting, darting, pricking, burning or boring character, which radiates along the course of a single nerve and its branches, recurring in paroxysms at short intervals.

To consider the significance of all neuralgic pains and their causes would lead through every department of internal medicine and of surgery. The first question to be decided is whether an existing neuralgia is symptomatic or idiopathic, i. e., whether it rests on a pathologic fundament (if so it is necessary to consider the nature of the primary lesion) or whether

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the neuralgia is idiopathic. There are also many other factors to be considered in deciding upon the prognostic significance of neuralgia. The following are among the more important factors which influence the prognosis of idiopathic neuralgia:

Neuropathic or Neuralgic Predisposition.—There are patients who after their childhood, which is usually characterized by marked asthenia, develop neuralgia in some part of the body on the slightest exposure to cold, sudden changes of climate, after insignificant effort or depressing conditions, or after slight strain or excitement. These patients are always *below par.* Women are oftener burdened than men with such *neuropathic tendencies;* with *menstruation, pregnancy,* and *during the climacteric,* they are made wretched by the recurring neuralgic pains which are not always limited to the same nerve. Unless the tendency is recognized early and corrected by such methods as lift the patients to the normal standard of health or above, they are likely to suffer throughout life. These subjects are almost always sensitive and emotional women of the better classes.

The influence of climatic change and rational living on prognosis in these neuropaths is paramount. Following the climacteric, often puberty, under favorable conditions with an improvement of the general condition, the neuralgias in these subjects cease, but are likely to recur on slight cause.

When this hyperesthesia which leads to neuralgia, is acquired, the prognosis as a rule is better than when there is a strong family history of neuralgia or other functional nervous diseases, for the acquired tendency is usually amenable to rational treatment.

Age and Sex.—Neuralgia is unusual early in life—rare before the tenth or twelfth year. Males suffer oftener than do females; in the latter neuralgias are often idiopathic; in men they are as a rule of organic origin. There are occasional periods when women suffer oftener than men. The cause of this variation is difficult to understand. Dividing our cases into five year periods and drawing an average, we find that women suffer oftener than men. Oppenheim and Bernhard however, from their large experience claim the preponderance of cases in men.

In young girls *abdominal neuralgias* and *"neuralgic headaches"* are favorably influenced by the establishing of normal menstruation.

Neuralgias in the aged are often dependent upon degenerative and nutritional faults (arteriosclerosis) which do not admit of successful treatment. Such neuralgias are associated with other symptoms of the underlying fault which make the cause clear and the prognosis easy.

In young and old, the prognosis of neuralgia is best in those cases in which the pain does not remain fixed. In both young and old, neuralgia in which there is evanescence of tenderness and acute pains in more than one nerve is not usually dependent on organic disease.

Anemia and Constitutional Diseases.—A frequent cause of all

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forms of neuralgia is simple *anemia,* or *chlorosis* which promptly yields to treatment.

The graver forms of anemia are more likely to have *anesthesias* and *paresthesias* (*Lichtheim symptoms*) than the ordinary neuralgias, though occasionally grave anemias are associated with persistent neuralgic pains. The prognosis for complete relief depends on the nature of the anemia.

Diabetes is often associated with pains of neuralgic character. Many of these are due to neuritis, and are persistent; others yield with the improvement of the general condition and the reduction of sugar loss.

Cachexias are at times associated with vague and irregularly distributed neuralgias without showing pathologic change on *post mortem;* these are likely to persist, though at times they disappear without known cause and do not return.

Infections, particularly *influenza, pneumonia, typhoid fever, measles* and *smallpox* during their early stages may have severe neuralgia which in most cases disappears with the full development of continuous symptoms.

Epidemics of neuralgia, described by Reilly and others, are unquestionably of influenzal origin; these yield to treatment.

The neuralgic pains of *syphilis* are, as a rule, due to neuritis, though occasionally it would seem that the toxemia is sufficient to cause neuralgia without organic change. This question is *sub judice.* The pain promptly yields to treatment.

Malaria may cause neuralgia in any part of the body; it observes some of the family tendencies of the disease including the periodicity of intermittent malaria. With acute malaria the pains yield promptly to treatment; with cachexia the course may be slower but unless malignant, complete recovery follows.

The neuralgias due to *poisons* are relieved if not chronic, by removal of the cause. These poisons include lead, arsenic, copper, mercury, alcohol, tobacco and phosphorus.

The neuralgias due to *masturbation, sexual excesses* and other *dissipation,* yield with the correction of the vice.

Bad habits, overwork, faulty housing, improper ventilation and exposure to cold, are all factors which invite neuralgia, which when controlled prevent recurrence and lead to cure.

In men, the larger nerves are involved (sciatic, etc.) more frequently, while in women the smaller trunks and their branches (intercostal, trifacial, etc.) are the seat of the pain.

When the nerve is tender to pressure during the first day or two of neuralgia, particularly during the paroxysms of pain, and the pain is limited to a single nerve, neuritis must be strongly suspected rather than simple neuralgia; these do not recover so promptly as do the idiopathic cases.

Pains (neuralgic) radiating along the intercostals and lumbar nerves

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after the fortieth year, should not be interpreted as neuralgic without considering the possibilities of bone (caries), spinal, aortic or visceral disease.

In adults, *crural pains*, continuous or paroxysmal, are rarely neuralgic; they are dependent upon pressure on the lumbar plexus, with knee jerk reduced or absent; this conclusion is strengthened and prognosis should be accordingly given.

The possibility of bone or other pressure should always be considered with *"fixed" neuralgia* which increases in severity from day to day, and the possibility of *metastases from distant organs* in which *primary growths may exist without causing symptoms (prostate, stomach, large intestine, etc.) should be remembered.*

Mild paroxysms are always favorable to speedy cure when not associated with marked *hyperesthesia* or *anesthesia.* With the latter, there is usually neuritis though there are exceptions to this rule.

Neuralgia with flabby and atrophic muscles is not as a rule idiopathic but of organic origin and the prognosis naturally depends on the cause and extent of the lesion.

Transitory tenderness along the course of the nerve is frequent with idiopathic neuralgia; the exacerbations of pain are associated with increase of tenderness.

Neuralgic pains about the head and jaw are usually dependent upon some discoverable cause which offers its own prognosis. The recognition of syphilis as a cause of neuralgia about the head with tender spots in the scalp leads to the relief of many. *Caries of the teeth* is the most frequent cause of pain about the face; to this I will again refer.

Neuralgic pains during the period of incubation of meningitis and the *radiation of pain along a single branch of the trigeminus during the early stage of brain tumor*, when there are no other evidences of disease, are not infrequent.

Nasal and frontal pains, neuralgic in character, can be correctly interpreted only after the examination of the sinuses and nasal cavities.

In deciding upon the significance of *persistent or recurring neuralgic pains in the thorax, the abdomen, and the extremities*, advantage must be taken of every possible aid, for after the thirty-fifth year the majority of these pains depend upon anatomic change. The reflexes are not to be ignored in prognosis, particularly in the unexplained neuralgias of women. Diseases of the heart, the lung, the abdominal viscera, the kidney, the genitals, associated with neuralgia, must be separately considered to make diagnosis and prognosis safe.

The hyperesthetic areas of Head will often prove of value for differentiation and prognosis.

The safe and scientific clinician will always brace himself against the diagnosis of idiopathic neuralgia, for he has learned that it is rarely jus-

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tified with increasing knowledge and refinement of diagnosis; its cause often exists within the nervous system itself and thorough search will reveal its presence. *Tabes dorsalis, spinal and peripheral growths, syringomyelia, syphilis of the spine, single and multiple neuritis and chronic spinal meningitis,* are among the causes of neuralgic pains without other developed symptoms.

Relapses.—Relapses with long intervals of freedom from symptoms are characteristic of idiopathic neuralgia, and offer a favorable forecast if the patient is not burdened with neuropathic tendencies.

Neuralgia which persists during long periods, in which paroxysms follow in rapid succession, are rebellious to treatment though cure often follows after years of symptoms.

Hysterical patients with neuralgic pains, indefinite as to paroxysmal recurrence and in which there is as a rule no "fixed pain," with marked development of the emotional element, "*psychoalgia,*" are often stubborn; the pains persist during long periods but finally yield to suggestion and rest.

Trifacial Neuralgia

(*Tic Douloureux, Neuralgia of the Trigeminus*)

The majority of trigeminus neuralgias are acute, severe, and depend upon diseased teeth, diseases of the nasal passages, bone or mucous membrane, exostoses, neoplasms, periosteal thickening or malarial poisoning, or persist without known cause.

In most cases but one branch of the fifth nerve is involved, though two may be painful at the same time depending on the location of the lesion. The fifth nerve is the most frequent seat of neuralgia. Conrad found it present 239 times in 717 cases of neuralgia.

Besides the usual manifestations of neuralgia including "*Valleix points,*" in severe cases there are secretory disturbances, spasms of facial muscles or auditory symptoms; the taste is disturbed and the general condition suffers.

Mastication in the chronic and many acute cases is impossible, and loss of weight is not unusual.

The acute cases run a favorable but painful course. The removal of the cause leads to prompt cure.

Neuralgia of the supra orbital branch is less obdurate than are the pains of the second and third branches of the nerve. When there is a *neuropathic fundament* the prognosis is materially influenced thereby.

Supra-orbital Neuralgia

Supra-orbital neuralgia due to *ocular defects* yields with the correction of the fault. Two-thirds of all trigeminal neuralgias are supra-orbital.

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With pain limited to the eye (*ciliary neuralgia*), search must be instituted for possible existing *glaucoma* or *optic neuritis, errors of accommodation* or other *diseases of the eye* which may cause ciliary neuralgia.

There is no more painful disease than neuralgia of the second and third branches of the trigeminus which becomes chronic (tic douloureux). It is almost impossible to determine the cause of this form of the disease; it may be *idiopathic* or *symptomatic,* it may be a symptom of grave disease, tumor, aneurism, osteoma, chalky concretions, disease of the nerves or of the Gasserian ganglion (Dana, Putnam, Horsely, Rose, Saenger, Krause, Keen, Spiller and Schwabe).

Operative interference and *injections* now extensively practiced, have relieved some of my chronic cases of tic douloureux during varying periods; the large majority have relapsed. It may be safely contended that *modern treatment offers longer periods of relief* than were formerly possible and make the disease more bearable, but *complete restitutio ad integrum is not frequently reached. Syphilitic cases* yield to treatment.

Chronic cases often continue during many years—twenty to thirty years, and longer. Senile and arteriosclerotic neuralgias select the trigeminus oftener than any other nerve, and remain unrelieved or cease without known cause.

There are cases of recurring trigeminal neuralgia in which the intervals are long and the cause remains unrecognized. These cases seem to run their course unrelieved by any known medical treatment and most recur in spite of surgical interference, though in some, the intervals have seemed to be lengthened thereby.

Occipital Neuralgia

Occipital neuralgia is, as a rule, symptomatic of either *infectious disease, arthritis deformans* (*spinal*), *spondylitis, gout, caries of the cervical vertebrae, syphilis, uremia, cerebral or spinal tumor, or ocular error.* With *neurasthenia, hysteria and muscular asthenia,* occipital neuralgia is frequent. The prognosis depends entirely on its cause.

The pain in the fully developed cases is bilateral (one proof of its organic cause). The occipital major branch is usually involved.

Intercostal Neuralgia

Intercostal neuralgia may prove to be the forerunner and accompaniment of *herpes zoster;* it is often of *reflex origin* in women with diseases of the uterus or its appendages (salpingitis, etc.); in young girls it is a symptom of *anemia* or *chlorosis.* Women suffer oftener than men. The left intercostals are oftener involved than the right. The *Valleix points* are present in most cases.

With persistent intercostal neuralgia organic disease should be sus-

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pected; caries of the spinal vertebrae, locomotor ataxia, spinal syphilis, aneurism of the aorta, angina pectoris, tumor of the cord, metastases from breast, stomach or other viscera must be excluded.

Hysterical women and oversensitive men often become self centered; they fear heart disease or other grave conditions.

The prognosis in uncomplicated cases is good; the pain yields to the treatment of the removable cause.

The *symptomatic neuralgia* depending on most of the conditions above mentioned makes the forecast unfavorable. Recovery of idiopathic cases is often slow.

Mastodynia

Sir Astley Cooper called attention to this painful neuralgic condition of the breasts in women—occasionally in men. The pain is aggravated during menstruation. Unbearable pain has been described by some of the sufferers. With the cure of the *menstrual* and *uterine anomalies,* the *anemia, hyperesthesia, faulty metabolism and assimilation,* and the *lowered vitality*—which are the usual causes—the pain ceases. *Enlarged and heavy breasts* at times continue hypersensitive and are only relieved by the removal of all pressure.

Phrenic Neuralgia

Peters called attention to phrenic neuralgia. The pains are described as radiating along the phrenic nerve, to the diaphragm. I have had no experience with this condition. The reported cases were associated with painful respiration and mastication, and were symptomatic of pericardial or cardiovascular diseases.

Kidd has reviewed the subject and Raynaud reported tuberculosis as a cause. Oppenheim says that in the absence of the lesions above mentioned the prognosis is favorable. He reports one case following fracture of the clavicle.

Brachial Neuralgia

Neuralgia of the brachial plexus may be due to one of many causes. My cases were often associated with *neuralgic and myalgic pains in other parts of the body,* especially in *gouty* and *diabetic* patients.

With diabetes, brachial neuralgia becomes fixed and rebellious to treatment even after the removal of all traces of sugar. *Arteriosclerotics* often have persistent brachial neuralgia.

Causes.—Syphilis, hypertrophic cervical pachymeningitis, tumors of the cord and the plexus, caries of the cervical spine, multiple metastases, neuroma, dislocation and fracture of the humerus and anchylosis, and angina pectoris are among the causes. In another group of cases anemia

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and the neuropathic habit alone explain the existing neuralgia. Unquestionably a number of cases are due to simple neuritis, lead poisoning, toxemia associated with the acute infections, malaria, distant visceral disease including gall-stones, and in one of my cases I found aneurism of the right subclavian during its incipient stage, the cause of persistent brachial neuralgia.

Oppenheim considers idiopathic brachial neuralgia a comparatively rare disease.

The prognosis depends on the ability to cure or remove the exciting cause.

Lumbar Neuralgia

Lumbar neuralgia involving the lumbar plexus may depend on *rheumatic or gouty conditions;* it is often a symptom of *disease of the cord or its membranes.* It may be due to *tumors or metastases,* including carcinoma, glioma, neuroma, sarcoma or osteosarcoma. Lumbar neuralgia may be an early symptom of *breast cancer with limited metastasis springing from the spinal bones,* and in some cases it was present before the breast growth was discovered.

Lumbar pains may precede the positive symptoms of *caries of tuberculous origin.*

The causes of *persisting lumbar pains are often explained by the x-ray examination.*

Rectal examination in unexplained cases may disclose conditions which by pressure (fibroid uterus, malignant growths, etc.) cause the pain.

Persistent double lumbar neuralgia should be considered to be of organic origin until it is positively proved to be idiopathic—a very rare condition. *Crural neuralgia* is usually (as already suggested in the general consideration of neuralgia) of organic origin dependent upon lumbar pressure.

Sciatic Neuritis

(*Sciatic Neuralgia, Sciatica, Ischias*)

Neuralgic pains within the domain of the sciatic nerve are almost always symptomatic of either neuritis or pressure, or are idiopathic, following exposure. This latter variety of sciatic pain may be considered to be very rare, for in most of the so-called idiopathic sciatic neuralgias, mild neuritis or perineuritis may be assumed to be present.

The *neuropathic tendency* is less in evidence than with neuralgia of the smaller nerves; the fact that the majority of sciatic neuritides are found in men, would explain the absence of a neurosis.

Gowers and Hyde believe that most cases rest on a gouty basis, and Ziemssen reports diabetic cases. I have not found it complicating diabetes as often as neuritis of the arms and legs.

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Double sciatic neuralgia is mentioned by Oppenheim as a complication of diabetes. I have never met a case; neither has syphilis been a frequent cause.

Causes.—Alcoholism, lead poisoning, acute infections, gonorrhea, sacroiliac synchondrosis tenderness and inflammation, lumbar myositis, exposure to cold and traumatism, chronic constipation and continuous pressure due to sitting on hard chairs are among the removable causes.

Every sciatic neuralgia which persists—particularly when double—should at once excite the suspicion of grave organic pressure, either tumor of the cord, metastases to the vertebrae (lumbar), extra-spinal pressure, growths within the abdomen, or spinal caries of tuberculous origin. I *have never seen a case of double idiopathic sciatic neuritis. These cases are always of organic origin.*

The *results of long continued sciatic neuritis* are atrophy of the muscles within the domain of the diseased nerve, spinal curvature, with the concavity toward the unaffected side, due to nature's effort to allow these patients to walk and relieve themselves of the pain at the same time.

Oppenheim calls attention to a condition, which I have frequently met, of reflex neurosis in which the general condition of the patient is lowered, there being marked asthenia, hysterical hemianesthesia, trembling, and other sensory disturbances.

The acute and rare idiopathic sciatic neuralgias run a satisfactory course, as a rule, with rest, though in some cases the duration is discouragingly long.

The subacute cases dependent on removable causes finally yield to treatment; but a sciatic nerve which has once been the seat of pressure or neuritis is ready in the future to revolt on slight cause—hence *relapses are to be expected.*

The *chronic* but *purely neuritic cases* may continue more or less troublesome during years; periods of improvement are followed by relapse, though cure is often possible.

Old patients recover slowly; they often suffer during long periods and die of intercurrent disease.

The prognosis of *symptomatic sciatic neuritis* depends on its cause. Most pitiful is the existence of those cases depending on primary growth with pressure or metastases, an easy *euthanasia* is all that our art offers.

II. Peripheral Neuritis

General Considerations.—Peripheral neuritis may be either (1) *single* or (2) *multiple*, and both of these varieties may be either *acute* or *chronic*. Neuritis may be *primary* or *secondary, interstitial,* or *parenchymatous.*

The *secondary neuritides* are either *syphilitic, tuberculous, cancerous,*

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or leprous. To all of these forms I refer in the separate chapters on these diseases, to which the reader is referred.

With both forms of neuritis there are degenerative changes. It must be remembered in offering a prognosis that reparative processes in the nerve are active, and that regeneration is possible. The wallerian changes are present with both forms of neuritis.

Most forms of neuritis, particularly the interstitial, are associated with inflammation of the perineurium, i. e., *perineuritis.* With the parenchymatous disease degenerative changes predominate over the inflammatory.

The *preaxial neuritis* of Gombaults offers a good prognosis. It is a mild type in which the axis cylinder remains undisturbed while there is a limited degeneration of the myelin substance of the nerve.

In the *chronic* and *progressive forms* of both simple and multiple neuritis the prognosis is influenced unfavorably by the disorganization of the axis cylinder, the replacing of the normal nerve structure by fatty and fibroid tissue, and the increasing changes in the perineurium.

Most neuritides are of the mixed type in their involvement of both the motor and sensory fibers of the nerve.

Single neuritis when it leads to paralysis, involves only the muscles within the domain of the inflamed nerve; *multiple neuritis* is characterized by paralysis of all four extremities in most cases (*quadriplegia*).

Mononeuritis

The leading features of single neuritis include pain and tenderness along the course of the nerve, anesthetic areas, trophic changes along the distribution of the nerve, muscular paralysis and atrophy, in accordance with the changes in the motor fibers.

Anesthesia and paresthesia are the most prominent features.

Traumatic Peripheral Single Neuritis

The course and prognosis depend on the *extent of the injury and the amount of destruction of nerve fibers.* Single neuritis following limited disturbance, contusion and compression, without break of continuity, may promptly yield in a few weeks—even sooner in exceptional cases. The more *severe injuries* with partial break of continuity *and associated paralysis* may require years for regeneration, or may never improve. If there is *complete separation,* restitution of function can only follow *surgical intervention.*

Sensory nerves improve faster after partial separation than do motor nerves. This is especially true of the fifth nerve.

Alcoholics who develop single neuritis after traumatism or exposure recover slower than do the temperate.

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The prognosis of traumatic neuritis following injury with paralysis depends very largely upon the ability to overcome pressure if present, to unite the severed fibers or place them in position to regenerate, and upon the condition of the paralyzed muscles as demonstrated by electric reaction.

The reaction of degeneration with severed nerves clouds the prognosis, but restitution of function may still follow after months of gradual progress. Experience with traumatic paralysis in children has been less favorable than in adults. Children, after the injury of nerves has led to paralysis, continue to neglect the function and form what Ehret called "habit paralysis." This "habit paralysis" has, according to some, been a powerful factor in the paralysis developed by infants during labor, but it may also account for paralysis due to other causes during the early years of life, particularly within the domain of the radial and ulnar nerves in which the child loses the "memory picture for the performance of movements, and with restoration of nerve conduction the function does not return" (Oppenheim).

Exposure to cold leading to single neuritis (facial paralysis—Bell's palsy) offers a good prognosis. The recovery may be slow, but unless there are associated conditions it may be expected with but slight remnant of the paralysis.

Single neuritis of secondary origin is frequent from extension of bone caries, joint disease, pressure of tumors, and syphilis, exostoses, dislocations of joints, and consecutive pressure.

Pressure of crutches is also a cause of neuritis.

The *occupational palsies* lead to limited neuritis. With all of these neuritides the *duration* of the disease, the *extent* of *anatomic change,* the *electric reaction,* and the *ability to remove the cause,* are the leading features which influence the prognosis.

With the *reaction of degeneration* the prognosis remains clouded and uncertain. If with this there is marked wasting of muscle, the chances for complete restoration are unfavorably influenced. *Early return to normal electric reaction is always favorable. Persistence of reaction of degeneration does not, as a rule, favor final complete return of function:* the paralysis may be permanent. In other cases the late improvement, under persistent treatment with the underlying cause removed, is occasionally surprising.

In occasional cases even with *partial reaction* of degeneration and limited atrophy the resulting paralysis remains permanent. *The rule should hold that with complete loss of electric response the prognosis for restoration of function is bad.*

Single neuritis, during or following the infections, usually yields after the effects of the original disease have been dissipated. With persisting treatment, the resulting damage in most cases is minimum.

Oppenheim and Siemerling call attention to the *hypersensitive state of*

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the peripheral nerves, caused by the acute infections and intoxications which invite neuritis in such subjects. These cases recover slowly with the improvement of the general condition of the patient.

Acute neuritis involving the facial, motor oculi, the *radial* and the *ulnar nerves,* usually runs a short course when not dependent on a permanent lesion. *Rheumatic facial paralysis* offers a good prognosis for prompt cure—from four to ten weeks (Lewandowsky).

Most single neuritides require a longer time for full recovery than do the uncomplicated or idiopathic neuralgias.

Postoperative Neuritis

The *mononeuritides caused by pressure* during surgical operations offer favorable prognoses. Persistent treatment is finally rewarded by success.

Paralysis following operations due to cerebral lesions are often serious. *Apoplexy, thrombosis,* or *embolism,* are the underlying pathogenic factors.

2. *Multiple Neuritis*

(*Polyneuritis*)

Single neuritides depend upon external causes, multiple neuritis as a rule upon internal or constitutional disturbance. Multiple neuritis is either of *infectious* or *toxic origin.* Occasional cases have been considered idiopathic, no cause being discovered. These will probably prove to be infectious or toxic with improved methods of diagnosis.

For a safe prognosis the etiologic factors deserve close consideration. Woodwork classifies the causes as follows:

"1. Acute specific fevers: diphtheria, influenza, leprosy, typhoid fever, scarlet fever and beriberi.
2. Poisons: alcohol, ether, carbon bisulphid, lead, mercury, arsenic.
3. Wasting conditions: diabetes mellitus, anemia, cancer and tuberculosis.
4. Exposure to cold or overexertion (probably due to some unknown infection, as febrile neuritis)."

To these may be added puerperal infection, abortion and associated sepsis, creosote, sulphonal, ergot poisoning, and arteriosclerosis.

The forms of multiple neuritis which interest us most and deserve separate consideration are:

(a) Alcoholic multiple neuritis
(b) Postdiphtheritic multiple neuritis
(c) Lead multiple neuritis

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(d) Arsenical multiple neuritis
(e) Multiple neuritis with leprosy
(f) Idiopathic multiple neuritis
(g) Landry's ascending paralysis
(h) Puerperal multiple neuritis.

(a) Alcoholic Multiple Neuritis

The prognosis of multiple neuritis caused by alcohol depends upon many factors. There are cases in which acute alcoholic poisoning leads at once to alarming and grave constitutional symptoms, which may precede *quadriplegic paralysis* by a few days, with marked *cerebral manifestations* early, *alcoholic meningitis, degenerative changes in the myocardium and liver,* and death within from seven to fourteen days.

In occasional cases *traumatism* in a chronic alcoholic suddenly leads to polyneuritis, with or without invasion of the sensorium. Without the evidences of "wet brain" such cases offer a better prognosis.

Another class of cases includes the *suddenly arising symptoms of quadriplegic paralysis* in those who after years of overindulgence discontinue the use of alcohol. In these subjects, without other constitutional faults and good resistance, the disease runs a favorable but slow course to recovery. Most of these cases are found in women who are steady drinkers.

Multiple neuritis developing in the course of delirium tremens has in *my experience proved to run a chronic course*—often rebellious. The majority of these patients recover.

Alcoholic meningitis and delirium tremens following shortly after the development of positive symptoms of peripheral multiple neuritis are among the most serious cases, and in the neglected who come to the hospitals from unfavorable quarters, who have been exposed to cold, pneumonia is a frequent complication, which usually with "wet brain," leads to death. With stiff neck and retraction the prognosis is unfavorable (Dana).

Meningeal symptoms are evidences of deep invasion of the sensorium, and add an element of danger.

The development of *Korsakoff's psychosis,* in which the patient is without memory for the events of the present but is able to recall the past, does not influence prognosis favorably; recovery is the rule but with the added psychosis the condition usually runs a chronic course, in many cases leading to full recovery.

In some cases which are neglected and bedridden during a long time, *bedsores* may lead to sepsis and cause death.

My experience in an active service has proved that the duration of the *ataxic cases* is longer than that of other types of the disease.

Pseudotabetic neuritis, in which there are marked sensory symptoms resembling tabes, are occasionally malignant.

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In many cases there are remnants of paralysis, though in most the functional ability of the extremities is sufficient to allow resumption of the original occupation.

The return of normal tendon reflexes, both patella and Achilles, is often long postponed: months and years may pass before these become normal.

Occasional cases of acute alcoholic neuritis of an ascending type, resembling Landry's paralysis develop rapidly, and promptly lead to death when they involve the respiratory centers. It is difficult to differentiate these cases from true Landry's disease, for they are acute and febrile, and at times foudroyant.

Alcoholic neuritis in the subjects of myocarditis, other serious heart lesions, nephritis or tuberculosis, offers an unfavorable forecast.

With grave constitutional symptoms, the resistance of the patient, his cardiovascular tone, and the extent of the brain lesions, are potent factors in the outlook.

The *extent of the paralysis* is not always an expression of the gravity of the disease. *Limited* polyneuritis and paralysis may be associated with grave constitutional and brain symptoms, while *fully established complete quadriplegia may run its course with but few added disturbances.*

All polyneuritides associated with tachycardia and dyspnea are serious, for vagus and phrenic involvement must be suspected, which is among the gravest of all complications.

The occasional association of optic neuritis or other ocular paralysis depends on some complication. The latter, according to Moritz, depends on *polioencephalitis hemorrhagica.*

The *extensive and marked tremor* does not influence the outcome unfavorably.

Relapsing cases are not uncommon, they are rebellious and may lead to permanent damage or cerebral complications.

(b) Postdiphtheritic Multiple Neuritis

(See Diphtheritic Paralysis in Chapter on Diphtheria, Section I)

(c) Lead Multiple Neuritis

Workmen in lead and those who have been poisoned through food or drink, or through one of the many other possible avenues from which entrance is possible, are differently affected. Unrecognized lead poisoning due to impregnated drinking water is a cause of indefinite symptoms as well as the prolonged ill-health, anemia, headaches, and lethargy of many within the precinct thus supplied.

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Children tolerate lead longer and better than do adults, but mental torpor and increasing lassitude with marked anemia characterize the chronic ill-health which finally develops. When fully developed *serious organic disturbances* with quadriplegia may follow.

Children develop *paralysis* of the lower extremities oftener than adults. Children of parents poisoned with lead may develop *epilepsy and other neuroses* as a direct result. The paralysis usually develops in the muscles most used, where it is more severe than in other parts of the body.

"Drop wrist" or *extensor paralysis* in the domain of the radial nerves is characteristic of lead poisoning. There may, however, as in all polyneuritides, be comeplete quadriplegia; it is not as frequent as with other toxic paraplegias. The *sensory disturbances* are less in evidence than with other forms of multiple neuritis.

The *severity of the poisoning* depends upon the extent of the changes produced. With marked blood changes, grave saturnine anemia, marked hypertension and arterial change, nephritis and lead encephalopathy the prognosis is grave. I have seen no case of lead poisoning in which chronic cardiovascular and kidney changes were overcome after once developed, though the paralysis in such cases may yield to treatment and removal of the cause.

The occurrence of *lead colic* and *"blue line"* do not argue against the possibility of recovery.

The sudden development of encephalopathy with either partial or fully developed paralysis is serious: it may lead to delirium followed by coma, symptoms of meningitis, and death.

The more favorable cases are those which develop soon after exposure to the poison and in which the early symptoms are recognized by the patient, and correctly interpreted by the attendant.

Chronic lead poisoning with paralysis, atrophy and the reaction of degeneration and beginning contracture offers an unfavorable prognosis for restitution of function.

The presence of the *reaction of degeneration* does not justify an unfavorable prognosis; most cases recover, if the source of poisoning is removed.

Repeated relapses materially influence the outlook unfavorably; these cases are aggravated by fresh poisoning, intemperance and overwork.

Months and years may be required before there is complete restoration of motor and sensory function in occasional cases.

Partial recovery with persistence of limited paralysis is not unusual. The peroneal muscles often continue weak and partially paralyzed.

Contractures in chronic cases are often permanent.

The arthralgias, blood conditions, cardiovascular and renal changes, encephalopathies, and colic, are separately considered (Intoxications).

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(d) Arsenical Multiple Neuritis

Arsenical muliple neuritis may be either *acute or chronic.* The acute cases are in the majority, though there are many chronic poisonings of which a number are never recognized, or even suspected.

Causes.—The poisoning results from the taking of arsenic by the mouth in some form—a single poisonous dose or large or badly tolerated dosage during comparatively long periods—through food, water, by inhalation from papered or painted walls or colored carpets, etc.

There are authorities who are active in their *opposition to salvarsan* because of the occasional occurrence of polyneuritis after its use. My own experience with the remedy which has been comparatively large, remains negative. It cannot be denied, however, that polyneuritis does occasionally develop after the injection of the remedy but should not be charged to it directly; it is one of the manifestations of syphilis possibly lighted into activity by a reaction following the administration of the drug, a *neurorecidive.* This verdict is entertained by Ehrlich who considers the phenomenon as a *Herxheimer reaction,* while others believe that the remedy first shows its poisonous effects in the nervous system. The faulty administration of the drug either in too large or in insufficient dosage may be the cause of direct poisoning or the Herxheimer reaction. In the latter event the intensive treatment with salvarsan and mercury cures the polyneuritis.

This entire question is still *sub judice;* it will require a larger experience and further observation before positive conclusions can be reached.

The *prognosis of the neurorecidive is not unfavorable.*

When the improper use of salvarsan leads to symptoms of acute arsenical poisoning with degenerative changes in vital organs (liver atrophy and kidney lesions), the prognosis is grave with or without polyneuritis.

Associated Symptoms.—Fully developed arsenical multiple neuritis is associated with *pains and paresthesia* in the hands and feet, at times arms and legs. *Paralysis with atrophy* is not long postponed. The early *gastrointestinal symptoms* are often troublesome—varying with the acute and chronic cases—in the former, with the amount of the poison taken.

Fully established paralysis is associated with the reaction of degeneration, hyperesthesia and anesthesia. The smaller muscles of the hands are oftener involved than with the other polyneuritides, and the contractures, when they occur, are characteristic (*paralysis chiropodale*). There is greater tendency to flexor paralysis than with alcohol or lead poisoning.

Pseudotabetic symptoms (ataxia) are frequent with motor paralysis. The patella tendon reflex is absent, and the resemblance of some chronic forms to locomotor ataxia may be striking (Dana). Oppenheim calls attention to *choreic symptoms* with ataxia.

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The trophic symptoms which accompany the motor and sensory symptoms are herpes (frequent), dermatitis, pemphigus, and pigmentation.

Bulbar symptoms are not frequent, though occasional, and with tachycardia present a serious condition.

The prognosis of most cases of arsenical polyneuritis is good. Recovery may at times be slow, occupying long periods, and complications may be added; but *recovery is the rule.* The *muscles last paralyzed are the first to resume their function.*

Fully established secondary contractures are likely to be permanent.

Serious complications include the infections, pneumonia especially, and myocardial degeneration.

(e) Multiple Neuritis with Leprosy

(See Leprosy—the anesthetic and mixed type.)

(f) Idiopathic Multiple Neuritis

(Infectious Multiple Neuritis)

Most forms of so-called idiopathic multiple neuritis are of *infectious* nature, now considered to be "rheumatic" by many. Osler characterizes it as *acute febrile polyneuritis.*

Temperature.—The *temperature* is at once high, reaching to 103° to 105° F. There are marked *cerebral symptoms, enlarged spleen,* and *albuminuria.* In most cases the *gastrointestinal symptoms* are alarming; *diarrhea* and *jaundice* are not uncommon.

Types.—The paralysis may be of the *ascending type,* or modified forms of paralysis; either paraplegia or quadriplegia predominate.

Associated Symptoms.—In most cases paralysis is preceded by sensory disturbances, anesthesias and paresthesias in hands and feet, and finally wrist and foot drop are in evidence besides involvement of the sensorium.

The *graver cases* include brain symptoms, phrenic and pneumogastric paralysis, dyspnea with respiratory paralysis, and tachycardia. The pupillary reflexes may be changed with Argyll-Robertson pupil.

In *rare cases* the cranial nerves, one or more, usually the motor oculi, facial or trigeminus, may be involved. In grave cases the resemblances to the Landry's form of poliomyelitis acuta (See Poliomyelitis) are close, and require differentiation.

The prognosis of the *idiopathic infectious form* of polyneuritis is grave. Death may occur during the first week or shortly after, particularly in cases with brain symptoms, respiratory paralysis, and heart involvement.

There are mild cases which recover slowly. In some the paralysis seems to remain unchanged during long periods, and then gradually improves; in others permanent paralyses remain. As a rule if the patients

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live beyond the acute period they make satisfactory recoveries, though often distressingly slow.

Jacobsohn calls attention to the prognostic significance of *complete reaction of degeneration,* in which he claims recovery of function is not to be expected in less than from four to six months. *Motor paralysis yields long before the return of the reflexes.*

Acute and threatening symptoms may arise suddenly, and seriously influence the outcome.

Aspiration pneumonia has been the cause of death in some cases.

(g) Landry's Paralysis

Classification.—In considering poliomyelitis I included in the classification two forms of Landry's disease; the *first* presenting sufficient features which justified the conclusion that it is identical with poliomyelitis. The *second* form includes those cases which are easily recognized during the first twenty-four hours by the increasing paralysis with less involvement of the respiratory muscles than in the first form, but in which there are all of the symptoms of fully developed ascending multiple neuritis before the end of the fourth day; in these cases the patients may live, but usually continue paralyzed.

It is impossible in the present state of our knowledge to subscribe to any positive conclusion concerning the pathology of these ascending types of paralysis.

All agree that the prognosis is exceedingly grave, that death is the usual outcome when there are bulbar symptoms, and that the few who live remain with large remnants of the original paralysis. At present I prefer to consider Landry's ascending paralysis as a form of *acute poliomyelitis,* to which chapter the reader is referred for further details.

Complications.—The multiple neuritides which are occasional complications of infections, acute and chronic, not considered in this chapter, receive attention in connection with the separate diseases to which the reader is referred.

Beriberi is also separately considered.

The prognostic data offered in connection with the consideration of alcoholic, lead, arsenic and the other forms of polyneuritis will serve to make clear the course of the paralyses with mercury, antimony, carbon bisulphid, morphin and coal gas poisonings.

Multiple neuritides of arteriosclerotic or cachectic origin (cancer and other tumors, leukemia, pernicious anemia, tuberculosis, etc.) offer an unfavorable prognosis.

(h) Puerperal Multiple Neuritis

Multiple neuritis following confinement is unquestionably an expression of infection. There are cases in which but one or two nerves are in-

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volved, the median and ulnar by predilection, but in most fully developed puerperal neuritides there is quadriplegic paralysis, with occasional Landry's complex and invasion of one or more of the cranial nerves. von Hösslin has reviewed the literature of this subject.

Seige reports the possibility of multiple neuritis during pregnancy, especially in cases of pernicious *hyperemesis.*

von Hösslin believes that the poisoning is often due to the dead fetus or retained placental remnants. The condition is always grave because of its dependence upon virulent infection.

(i) Gonorrheal Multiple Neuritis

Gonorrheal multiple neuritis selects the lower extremities by preference; it is at times associated with arthritis; vasomotor and trophic changes are often present, and persistent (Oppenheim). These cases are not frequent but are exceedingly rebellious to treatment.

(j) Neuritis of Tuberculous Origin

The neuritides of tuberculous origin have been separately considered (See Complications, Nervous Diseases, in Chapter on Tuberculosis).

(k) Diabetic Neuritis

Multiple neuritis due to diabetes mellitus is also separately considered among the complications of the disease (See Diabetes Mellitus). The prognosis is usually good in cases which are amenable to diet and other treatment.

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III. Peripheral Paralysis

The peripheral paralyses include:—

1. Paralysis of the cranial nerves
2. Paralysis of the nerves of the brachial plexus
3. Combined paralysis of the shoulder-arm nerves
4. Paralysis of the nerves of the lower extremities
5. Paralysis of the sacral plexus.

The causes and pathologic conditions which are mentioned in connection with all forms of neuritis and the neuralgias in the preceding chapters are included in the many factors which produce peripheral paralysis. In all, the prognosis is equally influenced. Hence repetition is unnecessary.

Neuritis is the leading cause of peripheral paralysis.

A break in a peripheral nerve may be due to a lesion located anywhere between the point of exit of its motor root from the brain or cord, to its terminal ending in the muscle.

Paralysis which is associated with a lesion of the motor ganglionic cells in the anterior horns of the cord should not be included in the peripheral diseases.

Peripheral paralysis in occasional cases is finally associated with cerebral and spinal lesions.

Paralysis of the Cranial Nerves

(a) Paralysis of the Olfactory Nerve

When loss of smell (*anosmia*) is due to removable causes, such as polypi, rhinitis, or acute inflammation, the prognosis is good.

When organic lesions cause disorganizing changes in the olfactory, these may be due to tumor, or other permanent lesions along its course and anosmia persists.

Syphilitic gummata may cause anosmia; the prognosis is favorable under treatment.

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Hysterical paralysis of the olfactory, causing anosmia, is associated with hyperesthesia of the nasal mucosa and usually yields to treatment.

Perverted smell (*parosmia*), is at times an *aura of epilepsy*, or it may be due to a lesion in the cerebral cortex.

Lesions of the olfactory bulbs with paralysis (anosmia) are usually permanent.

Atrophic changes with locomotor ataxia cause olfactory paralysis, which does not yield after it has persisted even a short time.

Hyperosmia is usually of hysterical origin and is likely to yield with the other symptoms.

(b) Paralysis of Optic Nerve

Amblyopia is a partial loss or blurring of the sight.

Amaurosis is synonymous with complete blindness.

Blindness of one eye may be due either to change in the nerve between the eye and the chiasm, either in the eye itself in the orbit at the optic foramen, or in the skull between the foramen and the chiasm. The prognosis depends on the nature of the lesion. As a rule, the underlying cause is either a new growth or some serious lesion. *Embolism of the central retinal artery* is among these.

The *blindness of one eye due to cortical lesions in the opposite hemisphere,* i. e., angular and supramarginal convolutions, unless dependent on syphilis or other removable cause, remains unchanged. For prognosis it must be remembered that there is in some cases of cortical lesion only partial blindness, but there is concentric limitation of the visual field, and the pupillary reaction is normal with cortical disease, but diminished with optic neuritis.

Hysterical blindness of one or both eyes offers a good prognosis. When the motor nerves of the eyeball are involved with optic neuritis, the disease is not due to a parietal cortical lesion.

Before offering a prognosis in a case of *bilateral loss of vision,* either partial or complete, it should be remembered that it *does not often follow organic disease of the nervous system as the result of primary or post-neuritic optic neuritis or optic atrophy* (Herter).

Errors of refraction without neuritis may cause amblyopia; the prognosis is good. Improvement almost immediately follows proper treatment.

Herter mentions *"functional amblyopia of one eye from irritation of the fifth nerve."* These cases depend upon carious teeth or other removable causes.

The lesions of the retina causing blindness are considered with the constitutional diseases upon which they depend. (Chronic and acute nephritis, syphilis, leukemia, the grave anemias, including malarial anemia and cachexia, diabetes, purpura, and the poisonings—lead, tobacco, alcohol, etc.).

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Optic Neuritis

It is difficult to offer a forecast from the presence of optic neuritis alone, as it is a symptom of many conditions. Foremost are those which increase *intracranial pressure,* including tumor and abscess of the brain, all forms of meningitis, encephalitis, syphilitic gummata and diseases of the cord.

Russell and Herter mention the rare occurrence of optic neuritis with myelitis and other spinal lesions without indications of cerebral mischief. Herter believes that it is to be regarded as "an associated and not a consecutive process."

The toxic and constitutional diseases mentioned in this chapter associated with retinal lesions, are also potent in causing optic neuritis.

Disseminated sclerosis of the optic nerve (retrobulbar disease) is a cause of neuritis often overlooked (because of the possibility of a negative ophthalmoscopic picture). In 6 per cent of all cases of multiple sclerosis optic neuritis is present, often slight and of short duration (Herter). Russell calls attention to the possibility of *advanced disease of the optic nerve without positive ophthalmoscopic evidence. The ophthalmoscopic picture of optic atrophy or neuritis is positive proof of organic disease of the nervous system, and in diagnosis and prognosis must always remain a powerful factor.*

Optic neuritis may exist without causing symptoms; with central lesions it is usually bilateral. When the neuritis *is most advanced at the optic papilla, the ophthalmoscopic signs of papillitis* are positive.

Optic Atrophy

Optic atrophy is usually *evidence of degenerative disease of the brain or cord;* including brain tumor, locomotor ataxia, is also found with diabetes and other constitutional diseases.

There are cases of *hereditary family optic atrophy* in which several male members of a family develop the disease after puberty.

It is impossible to separate the consideration of peripheral from the central cerebral and spinal lesions which are associated with lesions of the optic nerve and tract.

The Prognostic Significance of Hemianopia

(A loss of vision in one lateral or vertical half of the visual field)

Hemianopia is usually double; disease of one optic nerve may cause one-sided hemianopia.

Bilateral vertical hemianopia should always be interpreted as of organic origin, it may be either temporal, nasal or lateral, i. e., homonymous.

Temporal Hemianopia (or Bitemporal).—In this variety of hemianopia the temporal half of each eye is blurred. Such a lesion must of

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necessity include the decussating fibers of each retina, and is therefore located in the central portion of the optic chiasm. *If there is extension laterally* and the non-decussating fibers of one side of the chiasm are invaded, *blindness may result in the corresponding eye,* and *if there is sufficient extension as the disease (tumor usually) advances, to involve the opposite fibers, complete blindness results.* Locomotor ataxia, syphilis, abscess, brain tumor, osteosarcoma and chronic meningitis are among the *causes of bitemporal hemianopia.*

Hemianopia may occasionally prove to be functional, with migraine or hysteria. The characteristic attacks of the former, and the preponderance of the emotional element and variability of the symptoms in the latter, clear the diagnosis and justify a favorable prognosis.

Binasal Hemianopia.—This form is rare. The nasal half of each field being obscured, must of necessity involve each side of the chiasm in symmetrical lesions without impinging on the central fibers. Such condition has been found occasionally with vascular disease (small aneurisms) causing equal pressure, and with tabes dorsalis.

Lateral or Homonymous Hemianopia.—With lateral hemianopia, corresponding visual fields are affected: with right lateral hemianopia, both right lateral fields are blind; with left lateral hemianopia both left lateral fields are blind. The lesion must therefore be located back or behind the optic chiasm. This may be in one optic tract, in one of the lateral geniculate bodies, in the pulvinar of the optic thalamus, in the sensory tract of the internal capsule, in the angular gyrus with inclusion of the underlying radiating fibers, when there may be "crossed amblyopia" and mind blindness (Osler). Freund's *optic aphasia* may be associated with *mind blindness.*

Lesions of the cuneus, the occipital lobe or in the optic radiation may also cause lateral hemianopia.

To recapitulate: *Lateral hemianopia is due to a lesion which is located somewhere between the chiasm anteriorly and the occipital lobe and cuneus posteriorly (inclusive).* This includes the optic tract, the lateral or external geniculate body, the optic thalamus (pulvinar), the optic radiation, cuneus, the angular gyrus—occipital cortex. The lesion is located on the side opposite the obscured half fields.

The further exact localization must depend upon the associated symptoms. *Hemiplegia is a frequent attendant.*

Blindness in both eyes may be due to double lateral hemianopia—two lesions—one in each hemisphere—or to disease sufficiently destructive to involve the entire chiasm (Tumor, syphilis, etc.).

Lateral hemianopia may remain unchanged during many years in occasional cases. When it has existed for any length of time it does not again disappear. It may also develop in the course of migraine—rarely with hysteria.

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Further references to ocular symptoms and their prognostic significance are included in our consideration of the diseases of the spine and brain, the constitutional diseases, and those associated with faulty metabolism.

Paralysis of the Ocular Nerves

Causes.—The most frequent causes of paralysis of the ocular muscles are syphilitic gummata, locomotor ataxia, progressive paresis, compression due to neoplasms, acute infections including diphtheria, influenza and meningitis.

The *nerves which supply the muscles of the eyeball are the third, the fourth and the sixth.*

The results of paralysis of the ocular muscles, depending on the nerve, are *diplopia* (double vision) and *strabismus.* The latter is not always developed.

Congenital weakness is an occasional cause of *partial paralysis:* either the levator palpebrae superioris or the superior rectus is involved.

Congenital ptosis with the levator paralysis is materially improved by surgical interference.

The ophthalmic migraine of Charcot is probably epileptiform. It includes paroxysmal headache which spends its force in the eye and frontal region of the side affected, associated transitory paralysis of the motor oculi which disappears entirely between the attacks. The cause is unknown; treatment is without decided influence.

(c) Paralysis of the Third Nerve (Motor oculi)

Symptoms.—Ptosis, divergent squint and dilated pupil, with loss of accommodation, are the leading features. The symptoms depend upon the location of the lesion, its extent, and the branch of the nerve most involved.

In children the prognosis is not favorable, for *most cases depend on tuberculous meningitis, gliomatosis or cerebrospinal meningitis.* The *diphtheritic paralyses of the motor oculi* in children offer an excellent prognosis.

In the adult, the *idiopathic,* considered by many *rheumatic, and the postinfectious paralyses* lead to recovery in most cases. The *specific* (syphilitic) *paralyses,* yield to treatment, and are cured unless there are associated grave complications.

In *motor oculi paralyses associated with neoplasms* and other diseases, the forecast depends on the cause. Cases of locomotor ataxia with ocular paralysis are associated with the most chronic forms of the disease; they remain stationary during long periods (many years), and the patient learns to accommodate himself to the disturbed function. The *Argyll-Robertson pupil* is considered with *tabes dorsalis.*

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(d) Paralysis of the Fourth Nerve

The superior oblique being paralyzed, the eyeball is not readily moved downward and inward. *Convergent strabismus* is evident when the patient looks downward; there is also diplopia. Accidents from falling when the patient walks down stairs at times lead to the recognition of the paralysis.

The conclusions reached in connection with motor oculi paralysis are applicable for the prognosis of paralysis of the fourth.

(e) Paralysis of the Sixth Nerve

I consider the sixth nerve before the fifth, for the reason that with the third and fourth, it includes the trio of nerves, one of which is always included in paralysis of the muscles controlling the eyeball. The *external rectus is supplied by the sixth nerve;* hence there is convergent squint. *Diplopia* results when the patient looks to the side on which the muscle is paralyzed. When the lesion is located in the nucleus and not in the fully formed nerve, the opposite internal rectus controlled from the same source is paralyzed so far as it controls the lateral conjugate movement of the eyes; the patient is then without power to move either eye toward the side of the lesion. The internal rectus can, however, converge in conjunction with its fellow of the opposite side.

The prognosis of paralysis of the sixth nerve is the same as in that of the third and fourth nerves.

The clinician must remember that most paralyses of the ocular muscles depend upon lesions of the nerves (in which the nerve alone is involved) at the base of the brain. Occasionally a lesion at the base involves both motor oculi, usually tumor—malignant, tuberculous or gummatous; occasionally aneurism.

"Rheumatic" (?) neuritides are always one-sided, and offer a good prognosis.

The *ocular paralysis of tabes* considered above is usually nuclear, rather than peripheral.

(f) Ophthalmoplegia

Ophthalmoplegia is a condition in which all of the ocular muscles are paralyzed; ptosis is usually partial or may be complete. The eyeball is immobile. The *lesion is usually nuclear and chronic.*

Associated Symptoms.—It is associated either with tabes, paresis, multiple insular sclerosis, alcoholism, virulent influenza, carbonic monoxid poisoning, midbrain disease, tumors, hemorrhagic conditions, polioencephalitis—superior and inferior.

With some cases, multiple sclerosis especially, *nystagmus is present. These cases are slowly progressive and are not relieved by treatment.*

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There are cases of acute, and also recurrent or periodical, ophthalmoplegia. The *acute cases* may be hemorrhagic, occasionally diphtheritic. The latter offer a better prognosis than do the former. The *recurrent type of ophthalmoplegia* usually involves the muscles within the domain of the third nerve of one side. These cases are *periodic* and usually *begin with pain;* the headache and vomiting are severe; ptosis is frequent; the duration of the attack varies—the longer the interval between attacks, the longer will be the duration of ophthalmoplegia (average 3 to 6 weeks).

These *recurrent ophthalmoplegias are due to ophthalmic migraine; they are controlled with the greatest difficulty.* Occasionally life may be regulated or some factor is found which seems to control the symptoms, but as a rule, the recurrences continue during the active years of life, though may grow less frequent with advancing years or may remain uninfluenced throughout life.

(g) Paralysis of the Fifth Nerve (Trigeminus)

Primary disease of the trigeminus is not frequent; primary neuritis is rare.

Causes.—The leading causes are inflammatory diseases of the meninges, pressure due to neoplasms, fractures at the base of the brain and bone disease, aneurismal tumors pressing on the cavernous sinus, growths of the sphenomaxillary fossa and syphilitic gumma.

The trigeminus is composed almost entirely of sensory fibers except the third branch, in which motor fibers are included. The nerve supplies the skin of the nose and face to the median line, the mucous membrane of the nose, tongue and mouth very largely.

When both halves of the face and the mucous membranes are anesthetic, the lesion is located in the region of the gasserian ganglion upon which growths or metastases may press.

The *loss of sensibility* varies in accordance with the branch involved.

Pain is an early symptom which disappears, as a rule, with the increase of anesthesia.

Loss of taste and *trophic changes are frequent.* The former is limited to the anterior two-thirds of the tongue, when the lingual branch of the trigeminus is diseased between the peripheral distribution and its junction with the cauda tympani.

The trophic changes involve the cornea and conjunctiva; the cornea becomes dry and ulcerates; with cases dependent upon permanent lesions destructive processes are produced. *Herpes zoster* is also present, and is *evidence of disease of the gasserian ganglion or the nerve in front of it.*

The *motor paralysis* or weakness is due to disease which affects the third branch. *The muscles included are the masseter, temporal and external pterygoid.*

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Facial Hemiatrophy

Hemiatrophy of the face is a *rare disease;* there is atrophy of the muscles of one lateral half of the face with trophic changes in the skin and often in the bone tissue. The disease is found in the young, rarely after the twenty-eighth to the thirtieth year.

Cause.—The cause is unknown; in occasional cases the disease follows trigeminal neuralgia. Jacobsohn mentions the association of symptoms referable to the *sympathetic and associated papillary changes;* he also mentions the association with *trigeminal neuralgia of epilepsy, chorea and chronic spinal disease.*

Disease of the descending root of the fifth nerve has been considered by some to be the cause of this rare condition which remains entirely uninfluenced by treatment without threatening life.

Crossed paralysis of the fifth nerve (the fifth on one side, and the arm and leg on the other) is due to a lesion in the pons, and is usually due to vascular disease, neoplasm or a patch of sclerosis.

Carotid aneurism (internal), septic thrombosis, tumors of the orbit or cellulitis, and pituitary growths may cause paralysis of the superior maxillary branch.

Disease of the antrum and of the parotid may cause paralysis within the distribution of the second and third branches of the nerve.

The prognosis of paralysis within the distribution of the trigeminus is easily cleared in connection with a study of the previous paragraphs in which symptoms and causes are included. For satisfactory prognosis the individual case demands first of all the study of the primary cause; finally its location and extent, the amount of destructive change produced, and the ability to remove it.

Modern methods and early diagnosis lead to recovery in occasional cases but basal lesions, malignant growths, and chronic meningitides, are invariably hopeless.

(h) Facial Paralysis

(*Paralysis of the Seventh Cranial Nerve*)

Facial paralysis is the most frequent of all single nerve paralyses. *In considering the outcome of facial paralysis it is first necessary to have a clear understanding of the underlying pathologic lesion, and second to determine whether the disease is located in the upper or lower segment of the facial path. In other words, whether the paralysis is supra- or infranuclear.*

Character and Causes.—The character of the lesion and the causes are as a rule different with facial paralysis, in which all of the muscles of the face are involved, and in those cases in which the muscles in the lower half

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of the face are alone involved, which include mainly those above the angle of the jaw.

Bell's Palsy

(*Peripheral Facial Paralysis*)

Causes.—The most frequent causes of Bell's palsy are exposure to cold, disease of the middle ear, and caries of the petrous portion of the temporal bone.

When the facial nerve is affected, after its exit from the stylomastoid foramen, peripheral paralysis results, commonly known as Bell's palsy. The paralysis is often preceded by a period of neuralgia, due to neuritis or pressure. The characteristic facial appearance and changes are promptly recognized. There is an absence of normal wrinkling in the affected side, the eye does not fully close; the lower lid drops away from the eyeball; the tears fall down the cheek; when the cornea remains uncovered during long periods, ulcerative changes may follow. The nasolabial groove is effaced; the tip of the nose yields to the normal side; the angle of the mouth droops; the mouth is also drawn to the sound side. Whistling and distending the cheek on the paralyzed side are impossible. Sensation is unaffected; the tongue is not deviated. *If the nerve is involved within the fallopian canal,* besides the leading symptoms detailed in the preceding paragraphs, *taste is lost in the anterior two-thirds of the tongue because of chorda tympani pressure or disease.* In these cases there is usually suppurative middle ear disease with impairment of hearing and chronicity.

If the facial nerve is the only cranial nerve paralyzed, with normal sense of taste on the paralyzed side, then the disease is peripheral, outside the stylomastoid foramen, or possibly just within the fallopian canal. With a lesion of the facial nerve between its exit and the geniculate ganglion, there is paralysis with the usual symptoms, but no loss of taste. In these cases hearing is usually disturbed because the auditory nerve is likely to be involved by the same lesion. *Without this complication hearing may be hyperacute.*

Facial Paralysis Due to Pontine Disease

Associations and Causes.—This may be associated with paralysis of the sixth or other cranial nerves; usually hemorrhage, degenerative lesions with included bulbar paralysis, tumor or chronic meningitis, are among the causes. The pontine type of poliomyelitis may also cause this form of facial paralysis (See Poliomyelitis). The association of hemiplegia—simple or a crossed facial paralysis with hemiplegia—aids in localizing the lesion and determining the cause.

For prognosis after it has been decided that the paralysis is either peripheral or central, the pathogenic factor becomes paramount.

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The *peripheral facial paralyses have been considered by many to be "rheumatic;"* they often arise after exposure of the face to cold and in the majority of cases lead to complete recovery after a period of varying length.

The electrical response offers most valuable information in most cases of Bell's palsy. The prognosis is best for prompt recovery in the cases in which the reaction of degeneration is absent or but slight. Jacobsohn reports that in the absence of the reaction of degeneration the duration of the paralysis is from one to four weeks; with partial degeneration from one to three months, with complete reaction of degeneration, from three to six months. I have seen with the latter condition over one year lapse before recovery. Erb's and Oppenheim's experiences are practically the same. I have seen many exceptions to these experiences and agree that the electrical reaction is not always a guide to the prognosis of the paralysis, and that the severity of the lesion cannot always be determined by the electrical response in the individual cases. It remains, however, our most reliable guide for the prognosis of peripheral facial paralysis.

In many cases peripheral paralysis is without *prodromata;* it develops suddenly in such cases. *Uncomplicated Bell's paralysis rarely remains permanent.*

Recurrence is not frequent, but it does occasionally happen that repeated recurrences follow short intervals of normal function; finally permanent cure follows.

With *bone and middle ear diseases* which cause facial paralysis a guarded prognosis should be given. Unless the cause can be removed, return of lost function is impossible. *Syphilitic lesions causing facial paralysis* treated early, are favorably influenced.

Diphtheritic paralysis offers an encouraging forecast; almost all cases fully recover.

Fractures at the base, which recover, are likely, if the *facial is involved, to leave permanent paralysis.*

Mastoiditis, not too destructive, leads to final recovery of associated paralysis.

Growths in the mastoid, or of the face or ear, causing paralysis by pressure, lead to permanent paralysis unless they can be removed surgically, without inclusion of nerve fibers. The prognosis of injuries and division of the nerve depend on the extent and nature of the lesion, and the effect of surgical treatment.

Hemorrhage into the fallopian aqueduct, when absorbed, is followed by return to normal function.

Bulbar paralysis with facial involvement is incurable.

Hemorrrhage and softening of the pons is often followed by some improvement of the paralysis of the facial; naturally the extent of destruction varies in different cases, so also the prognosis.

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Tumors offer their own discouraging outlook, as do aneurismal dilatations causing facial paralysis.

The other infections associated with facial paralysis, also *alcoholic palsy,* offer an encouraging prognosis.

The differential points which are to be considered in the diagnosis of peripheral and central facial paralysis must also be considered in the forecast.

With central lesions, the upper neurons are involved, and the paralysis must therefore be of the opposite side of the face. *The voluntary movements of the face are lost while the emotional and reflex movement are but little, if at all affected. The upper part of the face escapes almost entirely.*

The electrical reaction remains normal or but slightly changed, and there is no reaction of degeneration. The tongue deviates to the side of the facial paralysis.

Aphasia with paralysis of the right side of the face may be present with hemiplegia. The hemiplegia with a lesion of the upper neurons and facial paralysis is on the same side as the facial paralysis; the lesion is supranuclear (above the facial neucleus).

With crossed facial paralysis and hemiplegia, the lesion is in the lower neurons or segment, *the lesion is on the same side as the facial paralysis; the hemiplegia opposite. The lesion is pontine.*

Double facial paralysis offers an unfavorable prognosis, for it is due, as a rule, to extensive pontine disease, chronic meningitis, tumor, hemorrhage, double otitis media—rarely with diphtheria or alcoholic neuritis. Cases have been reported with bulbar paralysis and erysipelas.

Facial paralyses with family neuropathic tendencies have been reported by Neumann, Charcot, Frey and Oppenheim, in several members of a family (brothers and sisters). These paralyses are likely to recur and are influenced by emotion (fright, worry, etc.).

Facial paralysis is a disease of mature life as a rule, most frequent between twenty and forty. *When found in children it is due either to diphtheritic paralyses, brain tumor, injury, syphilis, meningitis, or some other serious lesion. Barring an occasional case of facial paralysis due to diphtheria in children, the causes almost always include grave primary lesions, making recovery infrequent.*

(i) Facial or Mimic Spasm

Neurasthenic and hysterical children often develop facial spasm, which is usually rebellious to treatment and a *tic habit* may develop which is overcome with great difficulty and may never yield.

The *tic* which is associated with trigeminal neuralgia, particularly in old subjects, persists so long as does the neuralgia; sometimes in the aged

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and in young subjects it may persist after the relief of pain, or may develop as a sequel. Under these conditions it is likely to continue.

Tic may be purely reflex in character, at times from carious teeth, intestinal lesions, worms, polypi, diseased tonsils and lymphatics. If the cause is removable the tic yields. In children and young subjects the *shoulder and head muscles* are often involved. *Ocular errors* should be suspected; their relief cures some cases.

In women facial spasm, without other symptoms of chorea develops occasionally during pregnancy which bears no relation to a known pathologic lesion and disappears after labor.

Tic Convulsive

True tic convulsive is usually a *chronic spasm* of the muscles of one-half of the face, involving the orbicularis palpebrarum. Blepharospasm is present in most cases and as a rule, its pathologic fundament remains unrecognized. I do not include those cases which are due to cortical lesions in which there are spasmodic contractions of the facial muscles. Most cases of genuine tic convulsive are found in neurotic, overwrought individuals; in my experience the sexes have been equally affected.

Clonic spasms which predominate, may alternate with the tonic variety and are aggravated by excitement or emotion; they are often influenced by suggestion and may cease during short periods, particularly during rest.

The combination of tic convulsive with other neuroses is not infrequent. The French neurologists have reported the association of hysteria, neurasthenia, migraine, epilepsy and mental disturbances. The majority of my cases when complicated were found with migraine.

I have never been able to influence facial convulsive tic when fully established. The cases which have yielded were blepharospasm, due to ocular or other removable causes, some of the mimic spasms of children after long treatment in which environment proved a powerful factor. Occasionally I have seen facial paralysis develop in the muscles which seemed to tire out after years of spasm (Ballett).

Cases of mimic spasm following trigeminal neuralgia may cease after long periods without treatment.

The majority of cases of convulsive tic have not been associated with the explosive noises or psychic symptoms described by the French neurologists.

Convulsive tic does not affect longevity. The last three cases seen in private practice were seventy-two, fifty-six and about fifty years of age, respectively. The first of these had the spasm over twenty-five years before her death from cerebral apoplexy; the second is living and considers himself well after twelve years of tic, and the third is an active, healthy,

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The *tic* which is associated with trigeminal neuralgia, particularly in old subjects, persists so long as does the neuralgia; sometimes in the aged

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and in young subjects it may persist after the relief of pain, or may develop as a sequel. Under these conditions it is likely to continue.

Tic may be purely reflex in character, at times from carious teeth, intestinal lesions, worms, polypi, diseased tonsils and lymphatics. If the cause is removable the tic yields. In children and young subjects the *shoulder and head muscles* are often involved. *Ocular errors* should be suspected; their relief cures some cases.

In women facial spasm, without other symptoms of chorea develops occasionally during pregnancy which bears no relation to a known pathologic lesion and disappears after labor.

Tic Convulsive

True tic convulsive is usually a *chronic spasm* of the muscles of one-half of the face, involving the orbicularis palpebrarum. Blepharospasm is present in most cases and as a rule, its pathologic fundament remains unrecognized. I do not include those cases which are due to cortical lesions in which there are spasmodic contractions of the facial muscles. Most cases of genuine tic convulsive are found in neurotic, overwrought individuals; in my experience the sexes have been equally affected.

Clonic spasms which predominate, may alternate with the tonic variety and are aggravated by excitement or emotion; they are often influenced by suggestion and may cease during short periods, particularly during rest.

The combination of tic convulsive with other neuroses is not infrequent. The French neurologists have reported the association of hysteria, neurasthenia, migraine, epilepsy and mental disturbances. The majority of my cases when complicated were found with migraine.

I have never been able to influence facial convulsive tic when fully established. The cases which have yielded were blepharospasm, due to ocular or other removable causes, some of the mimic spasms of children after long treatment in which environment proved a powerful factor. Occasionally I have seen facial paralysis develop in the muscles which seemed to tire out after years of spasm (Ballett).

Cases of mimic spasm following trigeminal neuralgia may cease after long periods without treatment.

The majority of cases of convulsive tic have not been associated with the explosive noises or psychic symptoms described by the French neurologists.

Convulsive tic does not affect longevity. The last three cases seen in private practice were seventy-two, fifty-six and about fifty years of age, respectively. The first of these had the spasm over twenty-five years before her death from cerebral apoplexy; the second is living and considers himself well after twelve years of tic, and the third is an active, healthy,

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man in public life who has never been without facial tic since his earliest childhood.

I have not been able to confirm the conclusion of those who consider tic convulsive to be an evidence of degeneration.

(j) Auditory Nerve
(*Acusticus*)

Primary diseases of the auditory nerve are infrequent; rarely do we meet idiopathic neuritis of the nerve.

Causes.—*The leading causes* of auditory paralysis are tumor, hemorrhage, caries and meningitis. Cerebral syphilis, locomotor ataxia and neurorecidives (after salvarsan treatment) are also causes of acusticus paralysis.

Associated Symptoms.—*Labyrinthine invasion* may follow or be associated with the infections, including scarlet fever, diphtheria, typhoid fever, measles, otitis, parotitis, and other less frequent diseases.

Leukemia and pernicious anemia are occasionally associated with *labyrinthine vertigo or deafness.*

The anatomic structure of the auditory nerve must be considered, because there are in reality two distinct nerves, the *cochlear* and the *vestibular, each offers its own symptoms when diseased.*

Cochlear Nerve.—The *cochlear nerve* is associated more intimately with the *sense of hearing,* whereas the vestibular is connected with the vestibule and semicircular canals; its function is associated with the *maintenance of equilibrium.*

Invasion of both the facial and cochlear nerve is often present with many serious central lesions. These include locomotor ataxia, leukemia, aneurism, brain tumor, multiple sclerosis, caries, periostitis, syphilis and fractures at the base of the skull.

The *degree of deafness* depends upon the extent of cochlear change; when complete, bone conduction is lost as well as the detection of sounds through the air.

The *deafness which results from epidemic cerebrospinal meningitis is usually of cochlear origin,* is permanent as a rule, and in very young children is a cause of *deafmutism.*

Tinnitus Aurium

Tinnitus aurium is a frequent accompaniment of aural paralysis. Though a frequent symptom of auditory disease, it may be due to other causes—aneurism, cardiovascular and constitutional disturbances (chlorosis, grave or malignant anemias, uremia, acidosis and cinchonism). The significance of the symptom can only be decided after accurate diagnosis.

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Involvement of the Vestibular Nerve

Vertigo, impaired hearing, faulty equilibration and explosive seizures are the leading features of vestibular disease. Nystagmus is an occasional symptom.

Vertigo

Aural Vertigo

Labyrinthine Disease—Meniere's Disease.—Aural vertigo depends on some change in the semicircular canals, and is the leading type of true vertigo. *Nerve deafness, vertigo and tinnitus aurium are the predominant symptoms.*

Labyrinthine vertigo, or Meniere's disease, is associated with slight deafness, tinnitus aurium, vertigo, and recurring disturbances of equilibriation, which may be of sufficient severity to "throw" the patient.

Lesions and Symptoms.—The disease may arise suddenly from an acute labyrinthine lesion, or it may progress gradually. The *apoplectiform type is due to hemorrhage into the semicircular canals* and is associated with deafness of the ear involved. With tumor of the brain, osteosarcoma, facial and other paralyses are usually present also.

There are epileptiform seizures which are preceded by an aura including all of the symptoms of labyrinthine disease. Galvanization of the cervical sympathetic, acute diseases of the middle ear, inspissated cerumen, the sudden flushing of the external auditory canal with water, alcohol and tobacco poisoning may all give rise to the Meniere complex.

Neurasthenia and *hysteria* occasionally include Meniere symptoms which recur at short intervals, and are materially influenced by psychic factors.

Angioneurotic edema has in rare cases caused the Meniere complex with the acute onset of symptoms and their sudden disappearance (Lacharriere and Gescheit).

Locomotor ataxia and multiple sclerosis may be associated with true vertigo and symptoms which cannot be differentiated from labyrinthine vertigo.

I have mentioned the lesions and symptoms which are most frequent, for the reason that they give the data needed for safe prognosis. My experience with true labyrinthine vertigo has not been favorable for *restitutio ad integrum.*

Almost all cases run a chronic course in which, if uncomplicated by the serious organic changes which may cause the complex, the patient remains uninfluenced by any known treatment or the disease is progressive; hearing and equilibration are more and more involved, until the patient is incapacitated. In occasional cases with complete deafness the tinnitus and vertigo yield.

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The prognosis in those cases dependent on syphilis, ear, nose and throat diseases, and toxemias which are removable, is relatively good.

Hemorrhagic cases often yield to treatment. Occasional *epileptiform types* yield to intensive treatment, as do also the hysterical and neurasthenic varieties.

My presage is not so favorable as is that of Frankl-Holzwart, who holds that the prognosis of Meniere's disease is favorable and claims forty recoveries in seventy-four cases.

General Considerations of Vertigo.—Vertigo is frequent with organic, functional and nervous diseases, and the toxic states. There are cases of so-called *"essential vertigo"* in which no cause can be determined. It is never to be regarded as a disease *per se,* hence its prognosis can only be considered in connection with the conclusions which make clear the method and cause of its production.

Ocular vertigo is always associated with diplopia, *and yields with the correction of the error upon which it depends.*

Acute vertigo of gastrohepatic and intestinal origin *yields promptly to rest and treatment.*

Stomachal vertigo of Trousseau is often rebellious, but is finally favorably influenced by treatment. These cases demand close investigation, for often they prove to be true labyrinthine vertigo.

Epilepsy and vertigo, in which the latter is an aura, as a rule, recurs regardless of treatment, though favorably influenced by change of environment and methods of living, etc.

Petit mal with vertigo is exceedingly rebellious.

Chronic and acute uremia, acidosis, anemia and other constitutional faults in which vertigo is a prominent symptom offer their own forecast. Each of these conditions requires the close consideration of the underlying disease.

The *organic diseases of the brain,* of which vertigo is but a symptom, are usually multiple sclerosis, tabes, brain tumor and abscess, cerebellar ataxia, hemorrhage, embolism, thrombosis—all of these offer a doleful forecast.

In the so-called *"essential vertigo,"* persistent and repeated search for the toxic state, ocular errors, nasal and aural disturbances, and distant (uterine, ovarian, arterial, gastric and kidney) disease, often leads to happy results. *The possibility of migraine is not to be excluded.*

(k) Glossopharyngeal Paralysis

The leading features are loss of taste (ageusia), or perverted taste (parageusia) in the posterior third of the tongue, anesthesia of the back of the tongue and the pharynx, and (dysphagia) difficult swallowing.

Uncomplicated glossopharyngeal paralysis is so rare that its possibility is denied by many neurologists. The glossopharyngeal is involved with

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other nerves, with brain tumor, syphilis, chronic meningitis, aneurism and thrombosis of the jugular vein.

(l) Pneumogastric Paralysis

The *paralyses of the vagus* as it is associated with the separate infections and toxic states, and the prognostic significance of such conditions, are separately considered with the individual diseases.

Primary disease of the pneumogastric is exceedingly rare.

Compression of the nerve at the base, due to neoplasm (brain tumor), chronic meningitis, aneurism or caries, pressure anywhere along its course from enlarged glands, growths, inflammatory disease, intrathoracic pressure (aortic aneurism) causing paralysis of the recurrent laryngeal branch is easily recognized, and the significance becomes promptly apparent.

In considering *multiple neuritis and diphtheria and the poisonings* (tobacco, alcohol, lead, arsenic), I dilated on the effect of these conditions and called attention to the long periods during which the *tachycardia* due to vagus paralysis was tolerated. Most of these cases led to recovery.

With *alcoholic neuritis, arsenic, lead and phosphorus poisoning,* associated conditions clear the horizon for a reliable forecast.

Wounds which separate the fibers of the vagus usually *offer a grave prognosis.*

With *multiple sclerosis, bulbar paralysis, syringomyelia and locomotor ataxia,* pneumogastric paralysis once established, is permanent.

Cases dependent on *neurasthenia* and *hysteria* are often persistent, associated with many fears, but finally yield to suggestion and rational living.

Pneumogastric paralysis with ascending disease, Landry's paralysis (heart and respiratory symptoms), is uniformly fatal (See Poliomyelitis and Landry's Disease).

Tumors, injuries or diseases which cause paralysis of both vagi or recurrent laryngeal nerves are uniformly fatal.

Pharyngeal spasm is of hysterical origin—never organic. The presence of hysterical symptoms, the globus, the evanescence of the spasm make diagnosis and prognosis easy.

Cheyne-Stokes respiration is always a serious symptom and is associated with grave organic lesions separately considered.

Laryngeal crises of tabes have in a number of cases been favorably influenced by the modern treatment of syphilis.

(m) Paralysis of the Spinal Accessory Nerve

Growths located in the region of the foramen magnum are often responsible for paralysis of the spinal accessory and other cranial nerves.

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Nuclear change with progressive muscular atrophy and other organic lesions lead to the paralysis.

The symptoms vary with the location of the lesion.

Degenerative lesions involving the nucleus are associated with bilateral symptoms, and these are not limited to the trapezius and sternocleido mastoid. Bulbar symptoms are superadded. When the fully formed nerve is involved, the sternocleidomastoid and the upper portion of the trapezius are paralyzed. There is reaction of degeneration and atrophy.

Paralysis due to a lesion within the skull includes both portions of the nerve, the spinal and the accessory. The *nearness of the hypoglossal nerve and its inclusion in the process leads to paralysis of the palate on the side of the lesion.*

Paralysis of the sternocleidomastoid makes it impossible to rotate the head toward the normal side; no contraction of the muscle is felt when the attempt is made. *If both sternomastoids are involved,* the head tends to fall backward; it is bent forward with great difficulty.

With trapezius paralysis the shoulder on the affected side drops and cannot be normally raised. The arm is elevated with difficulty. The second and third cervical nerves send filaments to the trapezius which prevent complete paralysis.

Caries of the first and second vertebrae, cervical pachymeningitis, chronic meningitis, besides tumors and progressive muscular atrophy (above mentioned) and *traumatism,* are the leading causes of paralysis of the eleventh nerve.

Oppenheim acknowledges the possibility of *primary neuritis of the spinal accessory.*

Locomotor ataxia may involve the nerve; whether the lesion is central or peripheral is debatable.

Each of the causes mentioned in the preceding paragraphs makes prognosis possible. Surgical methods have been reported to relieve a few cases.

(n) Spasm of the Trapezius and Sternocleidomastoid (Spinal Accessory Muscles)

(*Torticollis, Wry Neck*)

Torticollis may be either functional or organic.

The *organic cases* of torticollis are due to suppurative disease of the tissues of the neck, glandular disease, neck tumors, injuries, and cellulitis. All of these are amenable to surgical treatment. With non-malignant disease the prognosis is good.

The *functional or spasmodic wry neck* represents *true torticollis,* the cause of which remains unrecognized in most cases, though in the majority

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there is a decided neuropathic diathesis, readily recognized. Most of my cases have been in young neurotic women and in children, though many claim that the disease predominates in the male. In the majority a hysterical element has been in the ascendency.

I have rarely met the *congenital torticollis* in practice in which the sternocleidomastoid is shortened; it is often degenerated, hard and resistant. *Tenotomy improves these cases.* Golding Bird contends that even after tenotomy "the facial asymmetry persists" and that "the facial asymmetry and the torticollis are integral parts of one affection which has a central origin, and is the counterpart in the head and neck of infantile paralysis with talipes in the foot" (Osler).

Symptoms.—The symptoms of functional spasmodic wry neck are readily recognized. The spasm may be tonic or clonic; these may alternate, or one type may predominate. In hysterical subjects there are long periods during which wry neck may persist and suddenly disappear to return on slight cause.

Causes.—Unquestionably wry neck may be caused by reflex disturbances due to uterine and ovarian disease. Among my cases is one, in which during many years the spasm recurred at short intervals, and continued during long periods in which an ovarian dermoid cyst was finally discovered and removed, with permanent relief of the spasm.

Course of the Disease.—There are cases which persist uninfluenced by any known treatment, either medical or surgical. One of my cases has subjected herself to innumerable surgical operations by the best surgeons in America without appreciable benefit. *The psychic influence of persistent torticollis is most depressing and makes many, particularly women of refinement with the neurasthenic habit, wretched, leading them to live the life of the recluse.* Life is not directly shortened by the disease save as the victims are led to suicide or develop a drug habit. The *acute form of the disease offers a good prognosis.*

Occasional cases of *muscular rheumatism* of the neck muscles (sternomastoid and trapezius) lead to several weeks of torticollis, which yields to treatment.

(o) Paralysis of the Hypoglossal Nerve

Most paralyses of the hypoglossal nerve are of *central and nuclear origin.* Lesions of the nerve after its exit from the skull are exceedingly rare. *Loss of power in the tongue is the leading symptom of hypoglossal paralysis.*

Causes.—When the lesion involves the nucleus, the paralysis is bilateral, as the nuclei of the separate nerves are close to each other. The lesion is degenerative in most cases. Bulbar paralysis, progressive muscular atrophy, syringomyelia, disseminated sclerosis, locomotor ataxia,

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hemorrhage, tumor, thrombosis, embolism, aneurism, caries, and chronic meningitis, are among the causes of hypoglossal paralysis.

Syphilitic gummata may cause hypoglossal paralysis; if unrelieved, the symptoms of tongue atrophy and paralysis persist. Such paralysis is likely to be one-sided, and includes the roots of the spinal accessory which causes paralysis of the larynx and pharynx on the same side (Herter).

With the bilateral paralysis of nuclear origin there may be labial paralysis also.

Crossed paralysis—hemiplegia on the side opposite the lesion with the hypoglossal paralysis on the side of the lesion—results from involvement of the fibers within the medulla. *Hemiplegia is present* in most, but not in all cases.

Neck growths and wounds occasionally cause hypoglossal paralysis, but these are rare, as are also the cases of *hypoglossal neuritis.*

Cerebral apoplexy is the most frequent cause of hypoglossal paralysis (Internal capsule with hypoglossal fibers involved).

The study of the underlying lesions which lead to hypoglossal paralysis detailed in the preceding paragraphs proves the limitations of our art in dealing with it. The specific cases are among those favorably influenced by treatment. Labial paralysis with atrophy once fully established is not likely to yield.

(p) Paralysis of the Phrenic Nerve

The anatomic relations of the phrenic nerve expose it to injuries and compression; arising from the third and fourth cervical roots it must naturally be included in *fractures and dislocations* of the corresponding vertebrae.

Causes.—Fractures, dislocations, spondylitis, tumors of the cord, caries of the spine, hemorrhage, cervical and cerebrospinal meningitis, myelitis, and other inflammatory conditions, are the leading causes of phrenic paralysis. Aneurisms of the thorax and neck also cause phrenic paralysis, and in occasional cases multiple neuritis (alcoholic, diphtheritic, lead poisoning and beriberi).

With multiple neuritis, if both nerves are included, it is a dangerous accompaniment, particularly if there are respiratory complications, such as pneumonia, bronchitis or pulmonary congestion.

Phrenic paralysis with lesion of the spinal cord is bilateral; usually other nerves are also involved.

Compression and crushing injuries are among the leading causes of bilateral paralysis.

When one phrenic is paralyzed, the diaphragm continues sufficient, but when both are included it is insufficient and powerfully influences respiration. The thoracic muscles attempt by increased action to com-

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pensate; the diaphragm is immobile. Dyspnea on exertion may become extreme.

The prognosis of paralysis of the diaphragm when bilateral is always grave, particularly with multiple neuritis and ascending paralysis, though recovery with the former condition is not impossible. The prognosis of phrenic paralysis due to the other causes above mentioned, is always influenced by the underlying lesion; it is usually unfavorable.

(q) Hiccough—Spasm of the Diaphragm

Hiccough is due to spasmodic contraction of the diaphragm. The efferent impressions are distributed through the phrenic nerve to the diaphragm, and through the laryngeal branches of the pneumogastric to the glottis.

Hiccough with inflammatory diseases within the abdominal cavity is always suggestive of grave disease, and in some cases of intestinal stasis indicates complete obstruction.

With peritonitis and appendicitis it is equally serious, and is usually associated with marked distension and sepsis.

With hernia—irreducible—it suggests strangulation.

With hemorrhagic pancreatitis it is associated with other symptoms; often collapse.

With typhoid fever it is almost always serious; it *may be a symptom of intestinal perforation, hemorrhage or deep toxemia.*

When not dependent upon peritonitis or perforation, hiccough indicates virulent infection and may persist during several days, materially weakening the patient, though it is not necessarily fatal. Cessation of long continued hiccough is possible, and convalescence from typhoid followed in a number of my cases in which the recovery was scarcely expected.

Hiccough due to rapid eating, hot or cold drinks, acute and transitory gastrointestinal catarrh, acute indigestion, and obstinate constipation is easily controlled.

Hysterical hiccough, at times persists during several days, but is finally relieved by rest and treatment.

Toxemia associated with hiccough is usually deep and threatening.

Hiccough with the *deep coma of uremia, acidosis, alcoholism and arsenical poisoning and profound meningeal toxemia is always a serious complication.*

(r) Paralysis due to Lesions of the Brachial Plexus

The causes of neuralgia and neuritis of the brachial plexus already mentioned (see *Brachial Neuralgia*) may also lead to paralysis of the plexus, or one or more of its nerves.

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Paralysis of all of the Nerves of the Brachial Plexus

Paralysis of all of the nerves of the brachial plexus is rarely due to neuritis; usually it is due to traumatism, to fractures of the humerus, or to dislocation of the shoulder.

Sensory and motor symptoms are combined. The extent of the paralysis must depend on the nerves involved. When, after dislocation reduction is long postponed, there is little likelihood of complete restoration of function; atrophy and some paralyses usually persist.

Prompt release of the plexus before degenerative changes have followed often leads to the full restoration of function. In all cases *alcoholism and other toxic influences reduce the chances of full recovery,* with complete plexus paralysis.

Surgical intervention has been efficacious in occasional cases.

(s) Paralysis due to Cervical Rib

Paralyses may be due to the presence of a cervical rib; there may be both *sensory and motor disturbances*—hyperesthesia, anesthesia and atrophy. The symptoms develop gradually. The presence of the cervical rib is not usually suspected because of the absence of symptoms before puberty.

The paralysis is more frequent in women than in men; the cervical rib causes symptoms in only a small proportion of cases (5 to 10 per cent). With a cervical rib on each side, the paralysis may be bilateral. Cervical rib may never cause symptoms.

The Röntgen examination clinches the diagnosis.

Oppenheim believes that cervical rib is a *stigma of degeneration.*

Surgical removal of the rib has been followed by relief of the nervous symptoms, including paralysis in a number of reported cases (Thorburn-Beck).

Paralysis of Two or More Brachial Nerves

Both the median and ulnar nerves may be paralyzed together in fractures and other injuries of the wrist. The musculospiral and ulnar, occasionally the musculospiral, ulnar and median, are injured or compressed by fractures of the humerus.

Paralysis of the brachial nerves may be either (1) *supraclavicular,* or (2) *infraclavicular.*

With (1) *supraclavicular paralysis* the shoulder muscles are included, with (2) *infraclavicular paralysis* the muscles supplied by the radial, ulnar, and median nerves, are paralyzed.

Erb's Paralysis—Supraclavicular Paralysis.—The supraclavicular, or Erb's, paralysis, is due to the involvement of the muscles which are supplied by nerves taking their origin in the *fifth and sixth cervical*

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roots, and include the deltoid, biceps, brachialis anticus, supinator longus, the supinator brevis, rarely the infraspinatus and subscapularis. The arm cannot be abducted because of the deltoid paralysis; the forearm cannot be flexed at the elbow because of the inclusion of the biceps, brachialis anticus, and supinator longus.

When the infraspinatus is paralyzed the arm may be rotated inward to some degree, but it cannot be rotated outward. *With subscapular paralysis* the arm cannot readily be rotated inward.

Anesthesia is frequent, involving the outer side of the arm from the deltoid to the hand, and the skin of the thumb, index finger, and the adjacent side of the middle finger.

The motor point where electrical reactions may be studied is located by Erb at the outer border of the sternomastoid muscle about two to three centimeters above the clavicle.

The prognosis of Erb's shoulder paralysis depends on the cause, the amount of atrophy, and the reaction of degeneration. The latter may be depended upon to give valuable indications, but should not be considered to the exclusion of all other factors. Complete cure or restoration of function with supraclavicular paralysis is exceptional.

The Duchenne paralysis due to injury of the child during labor is characterized by supraclavicular paralysis, as are also some cases following anesthesia due to pressure during the operation. In the latter cases the paralysis may be double. In the birth paralyses the diagnosis is often doubtful during long periods; with bone injury and paralysis complete restitution of function is unusual. Atrophic changes are likely to persist. *Plexus paralysis always offers a more serious prognosis than does paralysis due to single nerve involvement.*

Infraclavicular—Klumpke's Paralysis.—Paralysis of the muscles supplied by nerves taking their origin in the nerve roots of the eighth cervical and first dorsal roots are included in Klumpke's paralysis.

The hand muscles, the flexors of the wrist and the fingers are paralyzed. Sensory and vasomotor—trophic disturbances—are almost constant. The atrophy of the muscles with reaction of degeneration is in proportion to the severity of the lesion.

(t) Paralysis of the Posterior Thoracic Nerve

With paralysis due to a lesion involving the *posterior thoracic nerve, the serratus magnus is paralyzed.* Pressure due to loads carried on the shoulder, or injury, the acute infections, and the muscular dystrophies, are among the leading causes.

The symptoms include (1) "rotation of the scapula on its vertical axis when the arm is put forward, with recession of the edge of the scapula from the thorax—so-called 'winged' scapula; (2) the lower angle of the

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scapula is rotated inward and upward when the arm is carried forward; (3) the power of elevating the arm above the level of the shoulder is greatly weakened" (Herter).

The prognosis of serratus paralysis is not unfavorable when there is no break in the continuity of the posterior thoracic nerve; recovery is often slow.

(u) Paralysis of the Circumflex Nerve

Deltoid paralysis results from disease of the circumflex nerve; *abduction* is impossible save as there is some assistance from the teres minor.

One of the *results of circumflex paralysis* is the formation of *adhesion in the shoulder joint.* Many of these cases depend on single and multiple neuritis, and yield. Injuries, fractures and organic disturbances each offer their own prognosis.

(v) Paralysis of the Median Nerve

Paralysis of the median nerve alone is rare, and is usually due to traumatism. Injury of the stytoid process is a frequent cause (fractures, callus formation, dislocation, osteosarcoma).

When the paralysis is of short duration, atrophy slight, reaction of degeneration incomplete, and the cause removable, the prognosis is good.

Chronic cases after fracture and dislocation, faulty reduction, and callus formation, offer an unfavorable prognosis for restoration of function.

Symptoms.—The paralysis shows itself in inability to pronate the forearm fully; the wrist cannot be flexed toward the radial side; the thumb remains unopposed by the tips of the fingers. The second phalanges cannot be flexed on the first, and the terminal phalanges of the first and second fingers cannot be flexed; the third and fourth fingers can be flexed because of the intact ulnar half of the flexor profundus.

Long continued vasomotor and trophic changes with paralysis are unfavorable.

The *anesthesia* resulting from median paralysis includes the skin of the palmar side of the thumb, index, middle and adjoining half of the ring finger, the corresponding part of the palm of the hand, and the dorsal surface of the corresponding hand and fingers.

The muscles involved are: the pronator teres and quadratus, flexor carpi radialis, flexor digitorum sublimis, flexor digitorum profundus, pollicis longus and brevis, and the opponens pollicis.

(w) Paralysis of the Musculospiral Nerve. Radial Paralysis

Complete musculospiral paralysis includes the extensors of the elbow and wrist, the supinators and the extensors of the thumb and fingers. *In the common form,* the arm can be extended at the elbow, the nerve being

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involved lower, i. e., after the nerve has been given off which supplies the triceps.

Drop wrist is a frequent symptom of musculospiral paralysis in which the flexor muscles clearly show their ascendency by causing *contractions in chronic cases.*

If the lesion is sufficiently high to involve the *internal and external cutaneous branches of the musculospiral,* the back of the forearm and the outside of the upper arm are anesthetic.

Causes.—The musculospiral paralyses are often due to toxic neuritis, alcohol, lead, arsenic and other causes considered in the chapter on Multiple Neuritis.

Pressure paralyses within the domain of the musculospiral, when depending on transitory cause, offer a good prognosis.

(x) Paralysis of the Ulnar Nerve

Causes.—Fractures of the ulna and radius, injuries of the elbow joint external to the olecranon—oftener injuries of the forearm and wrist—are the causes of ulnar paralysis. Fractures of the humerus and dislocation, crutch pressure, and knife wounds are also among the causes. Fractures of the condyle may be followed after considerable periods by paralysis due to callus formation.

Occupation paralyses of the ulnar nerve are found among watchmakers, glassblowers, bakers, telephone girls and bicyclists.

Toxic and infectious disease (including syphilis, typhoid fever, sepsis, lead, arsenic, alcohol) are occasionally complicated with ulnar paralysis.

The *sensory paralysis* includes loss of sensation of the ulnar side of the back and palmar surface of the hand, the little finger, and the ulnar half of the ring finger and about one-half of the radial side of the same finger on the back of the hand.

The *muscles supplied by the ulnar nerve* are the flexor carpi ulnaris, flexor digitorum profundus, abductor pollicis, and the lumbricales and interossei.

Abduction and adduction of the fingers are impossible; the fingers cannot be flexed at the metacarpophalangeal joints nor can they be extended at the interphalangeal joints (Russell).

When the "claw hand" and interposed paralysis are developed, little hope even of improvement can be offered.

With long neglected bone injuries and dislocations the paralysis, atrophy, reaction of degeneration, and sensory changes, are usually permanent.

(y) Lumbar and Sacral Plexus Paralysis

The *causes of neuralgia* of the lumbar and sacral plexuses mentioned (See *Neuritis and Neuralgia*) are included among the causes of sacral and lumbar paralysis.

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Causes.—Compression due to primary growths and metastases involving the vertebrae, diseases of the pelvic organs, retroperitoneal masses, abscesses (psoas), inflammatory exudates, fractures of the pelvic bones, stab and gunshot wounds, dislocation of the hip, aneurism, gout, diabetes and poisonings (alcohol, neuritis and parturition), must all be considered as provocative of lumbosacral paralysis.

The nerves included are the:

Anterior Crural
Obturator
Sciatic
Gluteal
External Popliteal
Internal Popliteal.

Paralysis of the Anterior Crural Nerve

Symptoms.—With anterior crural paralysis there is atrophy and motor paralysis (quadriceps extensor); the knee cannot be extended, there is loss of patella tendon reflex, and with damage within the pelvis, the hip cannot be normally flexed while the knee cannot be extended.

The *anesthetic area* is on the front and inner side of the lower two-thirds of the thigh, the inside of the leg and the inside of the foot to the big toe.

(z) Obturator Nerve

With paralysis of the obturator nerve (derived from the third and fourth lumbar roots) the adductors of the thigh are involved; there is inability to cross the knees.

The nerve is rarely involved alone, usually with other lumbar nerves —occasionally after *difficult labor* in which there was long continued pressure. Such cases usually recover.

The anesthetic area corresponds with the upper third of the inside of the thigh.

(aa) Paralysis of the Sciatic Nerve

The symptoms depend on the seat of the lesion. *The prognosis is always bad with paralysis of both sciatic nerves,* or *evidences of pressure in which there may be full paralysis on one side, and gradually increasing symptoms on the other.*

Pelvic and lumbar masses with sciatic paralysis are always unfavorable.

I have seen a number of cases in which *metastases to the lumbosacral spine from carcinoma of the breast, stomach, intestine, prostate, and other organs were complicated, either early or late with sciatic pressure, the usual unbearable pains, and in the later stages fully developed paralyses.*

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In most cases of sciatic paralysis *there is paralysis of the muscles below the knee and anesthesia of the plantar surface, outer side of the foot and leg.*

With a lesion above the middle third of the thigh, the flexor muscles of the knee and extensors of the hip are paralyzed.

As suggested in the chapter on sciatic neuritis, *persisting symptoms referable to the sciatic nerve, one or both, must always create a strong suspicion of organic primary disease, and the prognosis can only be made after a thorough search for the pathogenic factor.*

(bb) Paralysis of the Gluteal Nerves

The paralysis within the domain of the gluteal nerves includes the gluteal muscles, pyriformis and the tensor of the femoral fascia.

The *superior gluteal nerve* arises from the lumbosacral cord, and its invasion causes inability to abduct or circumduct the thigh because the gluteus minimus and medius are included in the supply.

Paralysis of the gluteus maximus makes it impossible for the patient to extend the hip; it is impossible to rise from the sitting position, to climb hills or stairs.

With involvement of the superior gluteal nerve and paralysis of the gluteus maximus and the tensor fasciae, walking may be impossible because of the included inability to abduct or circumduct the thigh and the turning outward of the foot, due to the tensor fasciae femoris paralysis.

(cc) Paralysis of the External Popliteal Nerve

The external popliteal nerve supplies the tibialis anticus, extensor longus digitorum, extensor brevis digitorum, and peronei. When these muscles are paralyzed the ankle cannot be flexed and the first phalanges of the toes cannot be extended. There is "drop-foot," and as the condition increases *talipes equinus results, with anesthesia on the outer half of the front of the leg and the back of the foot.*

With *primary neuritis* the prognosis is good. Superficial injuries without break of continuity offer a favorable outlook. Fractures of the fibula and continuous pressure demand a guarded prognosis.

(dd) Paralysis of the Internal Popliteal Nerve

The ankle cannot be extended with internal popliteal paralysis and standing on tip-toe is impossible; the toes cannot be flexed, neither can the foot be everted.

If the lesion leads to *anesthesia* this is present over the outside and posterior surface of the lower part of the leg and the plantar surface of the foot.

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Most internal popliteal paralyses follow fractures of the tibia and fibula.

Paralysis of all of the nerves of the lumbar plexus offers a doubtful, often an unfavorable prognosis because of the underlying causes—tumors (abdominal), abscesses (psoas), metastases (carcinoma, osteosarcoma), and caries of the spine.

The suffering of these patients is often a factor in hastening death, and includes pains within the course of the genitocrural, ilio-ingual and iliohypogastric nerves.

Anesthesias may be irregularly distributed, and the paralysis includes the muscles supplied by the anterior crural and obturator nerves, in many cases.

(ee) Paralysis of the Sacral Plexus

With involvement of the entire plexus the prognosis is also grave, because of the associated pelvic lesion—malignant or inflammatory in many cases. *Rectal lesions* should also be suspected.

The *paralyses following prolonged labor and associated pressure* yield after variable periods in different cases; they are not frequent.

Primary neuritis and paralysis of the plexus offers a favorable prognosis.

When symptoms of atrophy, paralysis, anesthesia and degeneration follow a stage of pain or irritation, the prognosis is not encouraging.

(ff) Paralysis Due to Lesions of the Cauda Equina

Causes.—Most cauda equina paralyses are due to injury—crushing wounds, fractures—caries or malignant growths, causing pressure. The lesion usually causes bilateral symptoms, with approximation to symmetry, rarely one-sided symptoms.

Symptoms.—The symptoms are always suggestive of an intraspinous lesion, and are closely related with bladder, rectal and the sexual function in the male, with the characteristic distribution of the sensory disturbance and loss of patella tendon reflex.

The prognosis is easily made, for the history in most cases is clear as to the cause of the symptoms.

The rapid development of symptoms is characteristic of traumatism.

With gradually increasing symptoms, without external evidences or history of injury, tumor formation should be strongly suspected, and the forecast accordingly given. In these cases, the pain is severe in the region of the sacrum and down the legs. These symptoms are bilateral and symmetrical and include anesthesia about the rectum and genitals, bladder paralysis, atrophy of the legs, loss of knee-jerk, and spasm of the leg muscles.

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IV. Tumors of the Peripheral Nerves

Neuroma

The tumors of the peripheral nerves may be either *true* neuromata or the *false* neuromata. The latter are more frequent, and are usually multiple.

True neuromata are a part of the nerve structure, therefore intimately connected with the nerve, consist of nerve fibers and include ganglion cells. The occurrence of true neuromata without ganglion cells is doubtful.

The *false neuromata* are composed mainly of fibrous, myomatous or sarcomatous tissue.

The circumscribed and solitary growths of the peripheral nerves are either *benign* or *malignant.*

The benign solitary growths are the fibroneuromata, the neuromyxomata and neurolipomata.

The malignant growths include neurofibrosarcoma, secondary carcinomatous nodules (metastases) and neurofibromata, which finally degenerate and become malignant.

The neuromata which follow amputation are as a rule benign, but after removal they often recur.

Disseminated Neurofibromata—von Recklinghausen's Disease

Symptoms.—Disseminated neurofibromatosis is characterized by the development of multiple fibromatous masses of the nerve trunks or terminals, with multiple pigment deposits (naevi).

The size of the growth varies from an almond, or smaller, to an orange. In occasional cases there are similar deposits in the central organs, also Brain and Cord. My only case was not at all affected by the presence of the multiple masses and pigmentation. He presented no subjective symptoms. Wittman reports mononuclear increase in his cases, and Pierre Marie has seen cases of von Recklinghausen's disease develop cachexia and death, with symptoms of malignancy.

Multiple neurofibromatosis may be associated with *sensory symptoms,* including *neuralgia and paresthesia.* In some cases there are *psychic disturbances, malassimilation, extreme wasting, and other trophic changes.*

With central deposits the prognosis is always unfavorable.

There are *chronic cases* in which the disease persists without causing symptoms or shortening life; it may become stationary. Involution and cure is possible, though rare.

In some cases the disease is *congenital,* and several members of a

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family are affected. In these cases *other congenital defects are frequent* —muscle and bone anomalies.

Tuberculа Dolorosa.—*Neurofibromata which involve the subcutaneous branches of sensory nerves* lead to painful swellings (small and numerous) usually around the joints and breasts, easily palpable, and exquisitely tender. The condition is known as tuberculа dolorosa.

Plexiform Neuromata.—The plexiform neuromata are congenital and hereditary, as a rule. Separate nerve trunks are the seat of multiple growths; they may cause no symptoms and are rarely painful. In some cases all of the nerves of the body are included in the proliferative disease.

Elephantiasis Neuromatosa

Elephantiasis neuromatosa shows the characteristic picture of the elephantine leg with multiple neuromata of large size. There is enormous increase of fibrous tissue between the epidermis and the muscle fibers, and enlargement of the bones. *There is a strong tendency to malignant degeneration.* The disease begins in early childhood and progresses in cycles. There is no relief for the condition.

Naturally the histologic build and distribution of multiple peripheral growths influences prognosis.

Symptoms of central disease, severe and persistent neuralgias and the advent of cachexia are among the factors which presage an unfavorable termination.

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B. Diseases of the Spinal Cord

(*System Diseases*)

I. Diseases of the Afferent or Sensory System

1. Tabes Dorsalis or Locomotor Ataxia
2. General Paralysis of the Insane
3. Taboparesis
4. Herpes Zoster
5. Hereditary Ataxia (Friedreich's Disease)
6. Marie's Hereditary Ataxia.

1. Tabes Dorsalis (Locomotor Ataxia)—2. General Paralysis of the Insane (Paresis)—3. Taboparesis

The foregoing (1, 2 and 3) formerly classified as metasyphilitic diseases are known to be late manifestations of tertiary syphilis and are considered among the syphilitic diseases (See Syphilis of the Nervous System; Late Manifestations of Tertiary Syphilis).

4. Herpes Zoster

(*Shingles, Acute Posterior Ganglionitis, Zona, Zoster*)

Herpes zoster is an acute disease, probably hemorrhagic and inflammatory, involving the ganglia of the posterior nerve roots and associated with neuralgic pains in the corresponding nerves, which usually precede a vesicular eruption of the skin along the distribution of the nerve, the latter occasionally hemorrhagic.

The clinical significance of herpes labialis and vesicular eruptions with other infections have been separately considered (See Pneumonia).

Classification.—Herpes zoster is unilateral in almost all cases. The lay opinion that when the disease is bilateral ("meets in the middle") it is ominous and usually fatal, is unwarranted.

Occasionally there have been epidemics of herpes in which the prognosis was not different than in the sporadic cases. The most frequent forms of herpes zoster are intercostal, trigeminal (usually the ophthalmic branch), and cervicobrachial. Besides these, there are occipital, abdominal, lumboinguinal, sacrosciatic, and other localizations.

The *neuralgic pains* which precede the eruption of vesicles, as a rule diminish in intensity with their appearance.

The *vesicles and inflamed base* are often tender, and also cause inconvenience because of itching. The vesicles dry, usually cause no destructive

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changes save in exceptional cases, and after their disappearance leave brown spots which disappear after several months.

Confluence does not alter the favorable outcome.

The hemorrhagic form of zoster leads to limited destructive skin changes and permanent cicatrices.

With malignant cases, herpes may be gangrenous, and cause deep skin destruction with corresponding scars.

Duration.—The duration of the eruption and the healing process in the average case is three weeks; there are subacute cases in which there are repeated crops of vesicles which continue during several months. In anemic individuals, in those reduced by previous disease or diathesis, and in the aged, the *neuralgic pains may persist during months after the disappearance of the skin eruption and may recur on slight cause,* such as change of weather, excitement, and depressing factors. *Local hyperesthesia or anesthesia* may persist in occasional cases during varying periods.

Accompanying Symptoms.—Trophic changes may accompany herpes; these usually yield. *Herpes zoster involving the first* (ophthalmic or supra orbital) *branch of the fifth nerve* may cause ulcerative and inflammatory changes in the cornea and conjunctiva, rarely suppuration. With *complicating disease in other parts of the nervous system* there may be optic neuritis and Oppenheim reports paralysis of the motor oculi and the facial nerve.

Davidson reports *sacral herpes* associated with paralysis of the bladder and rectum.

Course of the Disease.—Herpes zoster which begins with elevation of temperature is usually endemic, occasionally idiopathic. These cases run a favorable course. The *majority of cases remain limited to a single nerve or plexus, and there is no tendency to multiple invasion* (many nerves). There is scarcely another disease in which the appearances and symptoms are so characteristic and uniform. *The prognosis is uniformly favorable.* The greatest dangers are from rare destructive eye lesions which may prove serious. These already mentioned, include *ulcerative keratitis, iritis and suppurative ophthalmia. When herpes accompanies the infections, its influence is not to be interpreted as unfavorable.* The chronic neuralgias in elderly patients are rebellious and recur on slight cause. Associated trophic disturbances usually yield after varying periods.

For a full consideration of the pathology of herpes zoster the reader is referred to the contributions of Head, Head and Campbell, Sherrington, and Howard (See references).

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5. Hereditary Ataxia

(*Friedreich's Disease*)

Hereditary ataxia does not long remain a system disease; combined or disseminated lesions are soon developed.

Friedreich's ataxia is a *family affection* in which several are affected —rarely one alone—*in which there is a combination of ataxia with motor weakness and characteristic deformities.*

The disease is not hereditary in the sense that it is handed down from generation to generation, but children of a father and mother in the same generation are afflicted.

There are a number of cases in which *epilepsy* and *mental diseases* have existed in near relatives, while Bouché considers *alcoholism* a cause, and Starr has seen cases *follow acute infections.*

The clinical history and pathology of the disease prove its progressive tendencies. The *changes are more far-reaching than in locomotor ataxia,* not only in the posterior columns, but also in the cerebellar tracts, the lateral columns, and the pyramidal tracts. *The greater changes are always in the posterior* (sensory afferent) *columns. Sclerosis* may extend to the peripheral nerves, and disseminated degenerative changes are extensive.

Symptoms.—The leading symptoms are motor weakness, nystagmus, speech defects, and absence of patella tendon reflex; Babinski is frequent, more or less curvature of the spine and cerebellar ataxia. The ataxia first affects the lower extremities and extends upwards.

Course of the Disease.—The disease as already mentioned is *progressive* until the patient is unable to maintain his equilibrium; he falls in a heap. Choreiform movements are frequent, ocular paralyses occasional.

With the advance of the disease there are *memory defects;* mental weakness is increased without sphincter involvement. Idiocy and labyrinthine vertigo are occasional.

Contractures of the lower extremities develop and resemble club-foot.

With Friedreich's ataxia *there is no Argyll-Robertson pupil, nor are there laryngeal or visceral crises.*

The progression of the disease is slow but certain; many unfortunates live incapacitated for years. The average age reached is between twenty and twenty-five years; Oppenheim reports cases which reached the thirtieth and even the fortieth year. Some die early in life of *acute infection,* particularly of pneumonia.

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Hereditary ataxia invites malignant infections. Diabetes is an occasional complication which promptly causes death.

There is no treatment which prevents the onward march of the degenerations. There are no cases of cure recorded.

Marie's Hereditary Ataxia

Marie described a form of cerebellar hereditary ataxia under the name of *"Heredoataxia Cerebelleuse"* in which the disease begins after the twentieth year with characteristic *cerebellar staggering.* The reflexes (patella tendon) are exaggerated, and the symptoms confine themselves entirely to the cerebellum without spinal invasion. In Marie's ataxia curvature of the spine and club-foot never develop. The disease remains unaffected by treatment, and is progressive.

II. Anterior Diseases—Diseases of the Efferent or Motor Tract

7. Poliomyelitis Anterior (Acute and Chronic)—Infantile Paralysis

Poliomyelitis is fully considered in the chapter on infectious diseases (See Poliomyelitis).

2. Landry's Ascending Paralysis

Landry's paralysis is considered in connection with poliomyelitis (See Poliomyelitis) among the infectious diseases and in the Chapter on Peripheral Paralysis (See Peripheral Paralysis).

3. Progressive Central Muscular Atrophy

Progressive central muscular atrophy is characterized by gradually increasing muscular atrophy which is dependent upon lesions in the cord, of a degenerative character, more particularly in the efferent motor tract, involving the gray horns (anterior multipolar cells) and the ventral horns as the disease advances, with change in the neuroglia. In these cases, though contractures and other symptoms of involvement of the lateral columns are absent, these nevertheless show atrophy and productive lesions. There is disappearance of the medullated fibers. This type is known as *progressive spinal muscular atrophy* or *Aran-Duchenne muscular atrophy.*

The greater changes in the lateral columns and anterior gray horns in some cases give rise to the *amyotrophic lateral sclerosis,* originally described by Charcot.

With involvement of the medulla oblongata its motor nuclei are involved, and *bulbar paralysis* results. I consider therefore:

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(a) Progressive (central) spinal muscular atrophy (Aran-Duchenne muscular atrophy)
(b) Amyotrophic lateral sclerosis
(c) Bulbar paralysis (Glosso-labio-laryngeal paralysis).

(a) Progressive (Central) Spinal Muscular Atrophy
(*Aran-Duchenne Muscular Atrophy*)

There are two forms of the disease: The *adult* and the *hereditary-family* or *infantile type.* In the latter type the leading anatomic changes are degenerative and are limited to the anterior horns and the peripheral nerves. The lateral columns are not as a rule involved.

Adult Type.—The adult type of progressive atrophy is found oftener in men and after the twentieth year, usually between twenty-five and thirty-five; muscular atrophies which develop before twenty or shortly after usually belong to the muscular dystrophies.

None of my cases have proved of specific origin, and heredity was not frequent. Osler reported a series of cases in which thirteen members of a family were affected in two generations; with the exception of two. The cases occurred or proved fatal above the age of forty and the late onset speaks rather for a central affection.

There are cases of *Aran-Duchenne atrophy* which during several years progress gradually, with all of the symptoms of the spinal form of the disease—in which there is *advance of degeneration to the motor nuclei of the medulla oblongata with glosso-labio-laryngeal paralysis—the patient rapidly fails.* One of my cases of this type remained purely spinal during almost two years but died within two months after the onset of bulbar symptoms.

The progression of atrophy is at first most marked in the interossei of the hands, and is symmetrical. The "claw hand" develops without paralysis but with increasing motor weakness and *fibrillary tremor, and never with hypertrophy of muscle tissue.*

The atrophy may remain limited to the hands during long periods. The disease finally gradually extends to the flexor arm muscles, later to the extensors. The reflexes of the arm are weakened or abolished entirely.

A reverse atrophy is not unusual; then the muscles of the shoulder or arm may be first involved. The disease may not progress to the lower extremities, or such invasion may be late.

The *unfavorable cases* so far as life is concerned, are those in which the respiratory center and the other motor nuclei in the medulla oblongata degenerate.

In another class of cases the *vagus center* may be suddenly involved and cause acute symptoms, i. e., *tachycardia besides respiratory embarrassment;* death is prompt.

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With progression the atrophy becomes extreme and the patient's appearance is characteristic. The skeleton is covered by skin and a small remnant of muscle.

Most chronic cases develop marked spinal *curvature and contractures.*

There is no true paralysis; there is a motor weakness only. In the later stages of the disease the weakness may simulate paralysis. There are but few exceptions to this rule.

Reaction of degeneration is incomplete; the *reduction of electric excitability* is in direct proportion to the extent of the destruction of muscle tissue.

Remissions have occurred in my cases during which the disease remained stationary for several years but progression followed; in some cases this was rapid and ascending. With the progression of symptoms there is increasing neurasthenia, often an hysterical element which adds enormously to the unhappiness of the patient.

Duration.—The average duration of the disease is between ten and twenty-five years. Fibrillary twitching is often evidence of advancing atrophy.

Many patients die of *intercurrent disease. Aspiration pneumonia* is a frequent cause of death.

Cure is unknown.

Juvenile or Family Type.—The juvenile or family (infantile) type of progressive muscular atrophy shows gradual progression of symptoms referable to the anterior horns and the peripheral nerves after the sixth month of life, at first limited to the thigh, pelvic and spinal muscles, from which the extension to the extremities follows in the course of several years. As the disease progresses the *reflexes are abolished* and the *reaction of degeneration* is a guide to the extent of muscle atrophy. There are no sensory symptoms.

Spinal curvature and deformity (*kyphoscoliosis*) develop as the disease advances.

Bulbar symptoms are not so frequent as in the adult type but are not impossible. A few cases are recorded in which bulbar symptoms preceded general muscular atrophy. The disease leads to death in from eight months to as many years.

(b) Amyotrophic Lateral Sclerosis

Charcot first called attention to the *association of disease of the anterior horns and lateral columns* of adults which usually attacks the cervical enlargement, and first includes *loss of power, atrophy and rigidity* of the upper extremities.

Course of the Disease.—The *first stage* continues from four to twelve

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months; *formication* with *contractures* and *exalted reflexes* characterize this stage.

As the disease advances and the cellular elements degenerate, the *reflexes are blunted,* the lower extremities are more and more invaded, rigidity, atrophy and contractures result with *fibrillary twitching.* The Babinski and Oppenheim symptoms are usually present.

In the third stage all symptoms are enormously increased, the reflexes are lost, and there are *bulbar* and *cerebral disturbances;* the general condition grows worse, *intercurrent disease, sepsis, pneumonia or myocardial degeneration* lead to death. *Atrophy, rigidity and motor weakness* are the leading features of the disease. The jaw clonus is easily obtained.

The disease is uniformly fatal, runs its course in from one to three years—rarely four—only occasionally longer; there are cases which lived ten years. Its *cause* is unknown; women suffer oftener than men, rarely before the twentieth or after the fiftieth year.

(c) Bulbar Paralysis

(*Glosso-labio-laryngeal Paralysis*)

The disease may limit itself to the motor nuclei in the medulla and pons or bulbar paralysis may be an early or late complication of any of the other types of progressive muscular atrophy in the adult. It may complicate multiple sclerosis and other grave organic central disease.

The degenerative type of bulbar disease is either *subacute* or *chronic.* The *acute form* is separately considered and it depends on a variety of causes. The chronic or usual form of bulbar paralysis is almost always associated with the lesions of the cord already mentioned.

There is a class of chronic bulbar paralysis in which the nuclear changes develop gradually and are due to arteriosclerosis, aneurism, or to the pressure of tumor or abscess.

Symptoms.—The separate symptoms due to the paralysis of the included nerves include defective speech (dentals and linguals) difficult swallowing with almost continuous salivation in advanced cases, labial symptoms, the large mouth and prominent lips, the return of food through the nostrils, feeble voice with laryngeal paralysis (*aphonia*).

The lip, tongue, pharyngeal and laryngeal paralyses offer the leading symptoms in the fully developed case.

Gradual progress is the rule; once developed the disease always leads to death in from one to three or four years.

Bronchopneumonia (aspiration pneumonia) was the most frequent cause of death in my cases.

Suddenly arising *tachycardia* with other symptoms of *pneumogastric paralysis* may end life suddenly.

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Acute Bulbar Paralysis

Acute bulbar paralysis is usually of vascular origin, apoplectic, embolic or thrombotic, with destruction of the motor nuclei (softening). It may be of infectious origin, as is pointed out in the consideration of the *bulbar and pontine types of poliomyelitis* (See Poliomyelitis); it may also be a sequel of *diphtheria*. A number of cases are recorded in which high voltage (electric shocks) have caused it.

Most acute cases are associated with *hemiplegia* or *crossed paralysis*.

The prognosis of acute bulbar paralysis is always grave. Occasionally a diphtheritic or typhoid case or poliomyelitis recovers.

Hemiplegics with bulbar paralysis, when the pneumogastric is not involved, may live during varying periods: *complete restitutio ad integrum* is not often to be expected. The same complication which ends the lives of those who suffer from the chronic form of bulbar paralysis—pneumonia—causes the death of most acute cases.

While death often follows *hemorrhagic cases* in a few hours or days, usually from aspiration pneumonia, respiratory or heart paralysis, the symptoms may improve and in rare cases there may be apparent return to health. This history is not often repeated.

Oppenheim has seen cases of acute bulbar paralysis recede in diabetic subjects.

Syphilitic cases not fully developed may also improve under rigorous treatment.

The cases of *acute bulbar neuritis* arising as a part of *multiple neuritis* are not frequent; they are of serious import, the prognosis depending upon the extent of the process; with *vagus paralysis* the outcome may remain doubtful during a number of days. *Complications including pneumonia* promptly lead to death. Comte has considered the clinical history of the neuritic form of bulbar paralysis (to which the reader is referred).

Bulbar paralysis with leukemia has been occasionally noted. The course of the disease is acute, ending in from two to six weeks.

Infantile Form of Progressive Bulbar Paralysis

The *infantile form* of bulbar paralysis was described by Fazio, Charcot, Londe and Brissaud. There are hereditary and family characteristics (Oppenheim). The disease, according to Oppenheim, develops in the children of consanguineous marriages and the paralysis shows early invasion of the upper fibers of the facial nerve with ptosis and ophthalmoplegia. The paralysis is associated with atrophy, lowered electric excitability, and the reaction of degeneration. The cases are exceedingly chronic unless acute infection causes early death. The juvenile form of bulbar paralysis offers nothing encouraging. In occasional cases there may be *congenital absence or defect of motor nuclei in the medulla.*

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Pseudobulbar Paralysis

Symptoms.—As a rule pseudobulbar paralysis *is not associated with atrophy of the lips and tongue* as is the bulbar paralysis. With pseudobulbar paralysis there are *symmetrical lesions* in the motor paths of both hemispheres localized in the cortex of the lower part of the ascending frontal convolution, or in the knee of the internal capsule. The lesions are therefore not in the medulla but are purely *supranuclear.*

Causes.—The underlying cause is usually arteriosclerosis of the cerebral arteries leading to multiple softening, hemorrhage, encephalitis and other local degenerative processes.

Course of the Disease.—*Hemiplegia* accompanies the bulbar symptoms which are apoplectiform. *Spastic conditions* usually develop. It must be remembered that there is no atrophy; there are often psychic disturbances, and these may be explosive with the development of the emotional element (laughing and crying); the muscles are not completely paralyzed and during emotion, automatically and by reflex action, these contract and are often overactive (Oppenheim).

The prognosis is bad; symptoms may persist during several years and may show some improvement, but do not disappear entirely.

Complications are frequent and are not well borne.

Infantile Pseudobulbar Paralysis

Probably these cases depend upon congenital anomalies or encephalitis. The prognosis is always unfavorable.

Myasthenia gravis
(*Asthenic Bulbar Paralysis, Myasthenia gravis pseudoparalytica*)

Erb in 1878 first called attention to a complex of symptoms purely bulbar—to which Oppenheim, Eisenlohr, Goldflam and Jacobsohn added marked muscular weakness—in which no pathologic lesion has been discovered to explain the symptoms; neither is the cause of the disease known.

The disease is found with almost equal frequency in the male and female, possibly slightly preponderant in the latter.

The enormous muscular asthenia increases with use and there may be final complete insufficiency.

The muscles within the domain of the *motor oculi, abducens, facial, glossopharyngeal, pneumogastric and hypoglossal* are usually included.

The asthenia may involve the laryngeal muscles.

The *paralysis* or *extreme exhaustion* after use may be transitory to recur on further effort, or it may persist. The latter frequently causes *ocular* and *laryngeal paralyses.*

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The *extreme fatigue* of the voluntary muscles is increased by *electric stimulation.*

Atrophy of muscles is only rarely present.

Most cases of myasthenia gravis begin with bulbar symptoms and gradually progress.

Ptosis and *double ocular paralyses* are frequent; the former is one of the usual symptoms of the disease, with *weakness of the muscles of the neck and jaw.*

The association of *Basedow's disease* (hyperthyroidea) is occasional.

The *neuropathic diathesis* has been prominent in all of my cases, while persistent thymus is frequent, and Weigert reported a thymus tumor with "thymus metastases" in the voluntary muscles involved. Congenital defects are numerous. Hun, Blumer and Streeter report "an infiltration of the muscles and of the thymus gland with lymphoid cells and a proliferation of the glandular elements of the thymus" (Osler).

The influence of the internal secretions on myasthenia gravis is not definitely settled (Biedl).

Remissions are frequent. These may continue from four to ten years; as a rule they are short. Most cases progress after remissions of varying length.

Recovery is not impossible though it is the exception. Oppenheim reports 26 deaths in 38 cases. Osler 180 cases, with 72 deaths.

4. *Progressive (Neural) Muscular Atrophy*

(*Charcot-Marie-Tooth Type of Muscular Atrophy, Peroneal Type of Neural Muscular Atrophy*)

Charcot and Marie, and Tooth called attention to a type of progressive muscular atrophy met as a rule during childhood—rarely after the twentieth year—which is of hereditary and family origin and stands on the borderline of central atrophy and muscular dystrophy.

Course of the Disease.—The disease begins during *childhood* in the peroneal muscles, and club-foot develops, either pes equinus or equinovarus.

The disease may not recur in the descendants of a family more than two or three times in from three to five generations. Jacobsohn believes that the disease may arise sporadically.

Extension to the upper extremities is not usual until the *atrophy and contractures* of the lower extremities have existed during many years. Rarely is the progress of the disease *reverse,* beginning in the upper extremities.

Sensory symptoms are frequent.

Fibrillary twitching is always present.

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Reaction of degeneration and reduced *electric excitability* are constant.

The disease is usually progressive; occasionally stationary. These periods vary in length but are followed by progression. The *duration* of the disease is from twenty to thirty years and longer.

The disease is of neural origin with involvement of the columns of Goll (Virchow, Friedreich, Oppenheim, Dercum).

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5. The Muscular Dystrophies

(*Progressive Muscular Dystrophy—Erb*)

The muscular dystrophies are in the majority of cases of *hereditary origin,* depending on primary lesions of the muscles, always *progressive,* though at times but slowly, characterized by wasting of muscular tissue, with or without hypertrophy, with final fat deposit in the connective tissue sufficient to cause *fatty degeneration, lymphatosis or pseudohypertrophy.* There may be true hypertrophy and pseudohypertrophy in the same muscle. As the disease advances, however, the hypertrophied muscle atrophies and the hypertrophic muscle undergoes fatty degeneration also.

The *hereditary factor* is paramount. With two sets of cases seen while writing this chapter, there was in one, a father and three children, in another a mother and two children, respectively—in all there were the characteristic appearances of the atrophic form of the disease. In the children there was primary involvement of the face (Duchenne infantile form).

Symptoms.—The earmarks of muscular dystrophy are, according to

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Oppenheim and Herter, the gradual development of the disease during childhood, the hereditary factor, the involvement of the muscles of the trunk, pelvis and lumbar region, the femur, the shoulder and the arm, the combination of atrophy, hypertrophy and pseudohypertrophy (fatty degeneration), the absence of fibrillary twitching, the absence of reaction of degeneration, and the quantitative reduction of electric excitability, and the characteristic movements of the patients when lying down as they seek to lift themselves. The patients stand with their legs spread apart and show a marked spinal curvature.

This classification of the dystrophies is accepted by Osler and reproduced in his Practice of Medicine (1913).

Course of the Disease.—As the disease progresses its characteristics are clearly manifested. The lordosis (curvature of the spine) is prominent. One case recently seen, the father of one group of the above mentioned cases, was about forty-five years of age and had the disease over thirty years. With marked lordosis, shoulder atrophy and involvement of the femoral and pelvic muscles, he is able to support his family as a postal official.

I. The Muscular Dystrophies of Childhood

1. *Hypertrophic Muscular Atrophy*

(a) The Pseudohypertrophic Form.—The pseudohypertrophic form is more frequent in boys about two to eight years of age. Pseudohypertrophic muscular atrophy is usually inherited from the mother, though she may not herself be afflicted.

Symptoms.—The "kettle calves" are characteristic. The gastrocnemii, glutei, quadriceps extensor, deltoid, triceps, supra- and infraspinati are all prominent and enlarged. The pectoralis major and the latissimus dorsi, at times atrophy. Lordosis is a late symptom. Reflexes are either abolished or weakened in accordance with the atrophy. With progression, while these patients walk fairly well on the level, they find great difficulty in going upstairs. One of my cases, a bright lad, was greatly disturbed because of his trouble in getting into the study room of his school on the second floor. All of these children arise when lying down by rolling over onto their hands and knees; the hands are moved to the knees and they manage to "climb up their legs." The waddling gait is characteristic and increases with progression of atrophy. In none of these cases are there sensory symptoms.

Classification.—It is a question whether it is wise to attempt to make an absolute differentiation of the various forms of the muscular dystrophies; the combinations are so frequent that at times this seems impossible.

Erb considers all the different types as *dystrophia muscularis progres-*

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siva and divides his cases into (I) those which occur in childhood, and (II) those which occur in youth and early adult life.

The Muscular Dystrophies of Childhood

I. Hypertrophic muscular atrophy
   (a) Pseudohypertrophic form
   (b) True hypertrophic form.

II. Atrophic form
   (a) Duchenne Infantile muscular atrophy (face primarily involved)
   (b) Without involvement of the face.

Juvenile and Adult Progressive Muscular Atrophy

(Dystrophia muscularis progressiva juvenum vel adultorum) (Erb's juvenile form).

These children rarely live beyond the twenty-third or twenty-fifth year. They usually die earlier of pneumonia or other infection.

(b) True Hypertrophic Form.—Most cases show the combination of the pseudohypertrophic with the hypertrophic form, and as the disease advances the true hypertrophy yields to atrophy or to fatty changes. This type, if its separate consideration is justified, will be found to be progressive, and shows the usual family characteristics of all dystrophies.

2. *Atrophic Form*

(a) With Primary Involvement of the Face (Infantile Form of Duchenne)—(b) Without Involvement of the Face.

These cases are all progressive, entirely uninfluenced by treatment, and show the leading features above mentioned, with, in almost all cases, the involvement of the shoulder muscles early.

II. Dystrophia muscularis progressiva juvenum vel adultorum

(Erb: *Juvenile Type*)

This type of muscular atrophy is rare. Its leading characteristics are its occurrence early during childhood, involving many groups of muscles in weakness and atrophy—the shoulder muscles particularly—the upper part of the arm, the pelvic girdle, the thigh and the back. The atrophy begins in the arm. The forearm and the leg muscles may escape. In these cases there may be pseudohypertrophy, or it may be absent. There is no fibrillary twitching. The reaction of degeneration is never found.

The Erb-Landouzy-Déjerine Type.—The Erb-Landouzy-Déjerine

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type of progressive muscular atrophy resembles the Erb juvenile atrophy; it has so many of the same characteristics that a separate division is hardly justified. The chief difference is in the muscles atrophied. This type, which is also hereditary, may be juvenile or arise in early adult life; the muscles of the face, shoulder and arms are mainly involved. The *"myopathic facies"* follows the involvement of the *orbicularis oris* and other *facial muscles.* The lips are separated, the lower lip abnormally prominent and the patient seems to "pout."

The *atrophy begins in the face. Pseudohypertrophy is rare;* some claim that it does not occur. The underlying cause of both the Erb and the Erb-Landouzy-Déjerine type is the same; for in the same family both forms may be present.

Complications of Muscular Dystrophies

Hysteria, neurasthenia and *epilepsy* may develop during the progress of the disease or may antedate it.

Idiocy and *psychic weakness* is occasional.

Medical literature includes other unusual complications, none of which I have met; they are *tabes, poliomyelitis, spastic paralysis, scleroderma, paroxysmal hemoglobinuria, Little's disease,* and *Friedreich's hereditary ataxia.*

The prognosis, so far as life is concerned, depends upon the complications and the time of the development of the disease. Respiratory complications (pneumonia) are unfavorable, as are also atrophic changes in respiratory muscles.

Early development is likely to lead to early death.

The infantile offers a less favorable prognosis for life than does the juvenile form of muscular dystrophy.

Cases which have lived to fifty years and beyond are recorded, as are also *abortive cases.* In some cases the disease may remain limited to the facial and shoulder muscles (Erb-Landouzy-Déjerine type), without causing serious inconvenience or affecting life.

The disease may cover periods of four or five decades.

The *development of contractures* may limit the usefulness of the individual.

Extreme lordosis with wide-spread atrophy or pseudohypertrophy are among the complications which lead to complete incapacity.

6. *Myatonia congenita*

(*Oppenheim's Disease* (1900)—*Amyotonia congenita*)

Oppenheim's disease is a *congenital degenerative process* in which there is *atony of the musculature* with the *flaccidity* characteristic of ad-

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vanced tabes, making *extreme flexion of the limbs possible.* The *voluntary movements are limited, making walking and sitting impossible* in the fully developed cases. The face is not involved.

The *patella tendon reflexes* are abolished. *Reaction of degeneration* is never found. The faradic excitability in the muscles is reduced, the strong interrupted current is easily borne.

Contractures of the lower extremities are developed in some cases.

Oppenheim has seen twelve cases.

The disease is unquestionably a myopathy which is rarely influenced by treatment though the prognosis is not absolutely bad, for a few cases have improved without complete cure.

Collier and Wilson who have analyzed the recorded cases, report that "there is always a slow and progressive amelioration."

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III. Lateral Diseases of the Cord

1. Primary Lateral Sclerosis

(*Spastic Paraplegia, Spastic Paralysis*)

Primary lateral sclerosis of the cord is an *infrequent disease* due to a symmetrical sclerosis of the pyramidal tracts, which is progressive, taking its origin in the connective tissue of these tracts; it is associated with more or less degeneration of the included tissue; the *nerve tubes* degenerate completely and often the anterior horns are involved. It is a disease of adult life; the age is usually between thirty and fifty; women are affected oftener than men. The cause is unknown.

The disease may attack perfectly healthy individuals, in some a congenital anomaly has been suspected to co-exist. In children spastic paraplegia has followed injury to the brain from the use of forceps.

Course of the Disease.—The progression of the disease is characteristic; it is uninfluenced by treatment. In typical cases there are three stages:

First Stage.—This stage is one of incomplete spastic paralysis in which the disease advances, while the patient is able to walk with the aid of canes. The reflexes are exaggerated.

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During the *second stage*—that of *complete spastic paraplegia*—there is increasing *rigidity* and the patient becomes bedridden.

The terminal, or third stage, is one of extension of the morbid processes with *muscular atrophy, bed sores and cystitis. Intercurrent disease* is usual.

The weakness of the legs which involves the flexors of the hips, knees and ankles may increase gradually, almost unnoticed during many years. At times in its progress it is greater in one leg, but with the advance of the disease it affects both extremities. The arms are only rarely affected. The other characteristics of primary spastic paraplegia develop as the disease progresses and include *exaggeration of the knee reflex* and *ankle clonus; the extremities become stiff and unyielding, the gait characteristic;* two canes are required; the *tottering* from side to side of the ataxic is absent; watching the ground is unnecessary; there is no run or trot as in paralysis agitans.

Paresis increases with rigidity.

Symptoms of Advanced Spastic Paraplegia.—The trio of symptoms to which the disease advances are:

(a) Stiffness or rigidity
(b) Paresis
(c) Exalted Reflexes.

The *Babinski symptom* is present, also tremor or spasmodic twitching, and exaggerated abdominal reflexes. The atrophy of the muscles is due to advance to the anterior horns. The *Oppenheim symptom* is also present.

Uncomplicated cases show no sensory symptoms nor sphincter weakness save in exceptional cases; neither is there reaction of degeneration.

The disease may show *stationary periods* during any one of its three stages. It does not of itself destroy life which may continue from ten to forty years, the patient remaining bedridden during most of this time.

Like all system diseases there is always great tendency to involve other systems of the cord, with extension to the brain and peripheral nervous system. Anterior and posterior sclerosis are among the most numerous of such extensions.

2. *Congenital Lateral Sclerosis*

(*Little's Disease*)

Cause of the Disease.—In the majority of cases the disease is due to a combination of lateral sclerosis with a cerebral lesion, usually encephalitis (non-suppurative).

Symptoms.—In almost all cases the symptoms of rigidity are apparent shortly after birth, though there are exceptions to this rule. The diagnosis may not be made until the child attempts to walk when *spasticity of gait* is characteristic. There is with rigidity some motor weakness.

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Patella tendon reflex is exaggerated, ankle clonus may be absent. As the symptoms develop fully, the patella is prominently pushed forward and the ligament of the patella is elongated. Babinski is present. Sensory and sphincter symptoms are absent. In most cases the spastic condition is limited to the lower extremities, though the arms are occasionally included.

Forecast.—The *hereditary foundation* of almost all cases clearly established, makes the forecast for complete cure unfavorable.

The diplegic character with the other symptoms of the disease accents the cerebral involvement, and also darkens the prognosis in pronounced cases. There are cases which are attributed to injuries during labor (forceps, pelvic pressure, etc.), and which present no more favorable prognosis so far as restitution of function is concerned than do the others.

Athetosis, epilepsy, dementia, chorea, speech and ocular defects are among the associated conditions, none of which are amenable to treatment.

The cases are most favorable which at birth or shortly after show but limited rigidity without marked paraplegia. Slight paraplegia may not advance, and with education and mechanotherapy, improvement may result; such children become useful, able to help themselves and learn to walk.

The disease may remain stationary.

Surgical interference in individual cases has improved function, and usefulness of the extremities has followed.

While the condition may improve materially, there is in the most favorable cases a remnant of rigidity which is never entirely overcome.

3. Combined Lateral and Posterior Disease

(*Ataxic paraplegia*)

Ataxic paraplegia depends upon sclerosis of both the lateral and posterior columns. In these cases the dorsal columns are mainly involved, the lesions in the lateral columns show marked diffusion. Vascular changes in the cord are frequent.

It is questionable whether ataxic paraplegia is ever primary; the cases which I have seen disprove that possibility almost completely. There are those who believe that some cases rest upon a marked neuropathic disposition.

Associated Diseases.—In the order of frequency I have found, from experience and literature, the following diseases associated with combined posterolateral disease:

1. Arteriosclerosis
2. Pernicious anemia
3. Toxemia
4. Lead poisoning

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5. Malarial cachexia
6. General paresis
7. Leukemia
8. Pellagra (My own experience with pellagra is too limited to justify conclusions).

Course of the Disease.—The symptoms of fatigue are soon followed by more or less unsteadiness and marked incoördination and the Romberg symptom. The patient walks with canes and watches the ground; there is less rigidity than in uncomplicated lateral sclerosis—no pain as a rule—but with the anemias there are often paresthesias and anesthesias.

The disease as it advances leads to *sphincter paralysis.*

When there are *mental symptoms* the process is advanced.

I have recently seen one case of pellagra in which, under treatment, the symptoms including *marked mental disturbance* yielded to treatment.

The *reflexes* depend entirely upon the extent and location of the disseminated lesions.

With advance of the tabetic element and lesions, there are *pupillary and optic disturbances* which usually persist uninfluenced.

Forecast.—The symptoms of either spastic spinal paralysis or of ataxia may predominate, and the reflexes as above suggested are accordingly influenced.

The primary disease must of necessity influence the prognosis, hence in considering the diseases with which ataxic paraplegia is associated, I have no encouraging forecast to offer. Grave anemias (bothriocephalus, etc.) amenable to treatment, are followed by improvement. These cases are rare.

Duration.—The duration varies. The average case rarely lives beyond two years. The underlying cause will make it possible for the clinician to give an approximate opinion of the possible duration in the individual case.

4. Amyotrophic Lateral Sclerosis

(*Charcot's Disease*)

See Anterior Disease of the Cord.

5. Erb's Syphilitic Spinal Paralysis

See Syphilis of the Cord (Chapter on Syphilis).

6. Secondary Spastic Paraplegia

Course of the Disease.—With transverse lesions of the cord above the lumbar enlargement, motor paralysis is finally complicated with the characteristic symptoms of spastic paraplegia below the level of the lesion.

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Spastic paraplegia in these cases shows increased myotatic irritability, exaggerated patella tendon reflex and the presence of ankle clonus. The paralyzed legs become rigid and contractures are frequent. In these cases there is always secondary degeneration in the pyramidal tract which cannot be prevented by any known treatment.

Causes.—These secondary paraplegias may follow long continued pressure from injury, tumor, metastases, caries, myelitis, meningitis, hemiplegia, meningeal hemorrhage, or other bilateral cerebral and spinal diseases.

Once established secondary spastic paraplegia remains uninfluenced by treatment; the length of the patient's life depends upon the nature and extent of the cause.

7. Amaurotic Family Idiocy

(Sachs' Disease)

Symptoms.—B. Sachs, in 1903, called attention to a form of *spastic paralysis of distinct family type* associated with idiocy, which appears usually in the first or second year of life, is limited to Jewish children and is progressive.

The paresis leads to paralysis of the extremities and may finally become flaccid though rigidity may continue.

The *reflexes* are usually exaggerated though they may be decreased or abolished.

The *amaurosis* is characteristic. At first the blindness is not complete, but as the disease advances sight is entirely lost. The change in the macula lutea is also characteristic—a red spot is seen with a white patch of surrounding atrophy.

The children show their *mental weakness* early; *the progression to complete idiocy is surprisingly rapid. Nystagmus, strabismus and aural defects* are also found in some cases.

Death is preceded by marked *marasmus.*

The *duration* of the disease is about two years. The *course of the disease* remains uninfluenced by treatment.

Cause and Pathology.—The true cause and positive pathology of the disease are unknown. Sachs believes that the pathologic changes include the *primitive type of the cerebral convolutions, macrogyria, degeneration of the large pyramidal cells, decrease of the fibers of the white matter, and absence of tangential fibers* (Osler). On the other hand, Schaffer contends that the disease is of *postpartum origin,* advances because of insufficiency and inferiority of the nervous system, that the ganglionic cells undergo degenerative changes and exhaustion while there are atrophic changes in the cerebrum, in the subcortical ganglia and in the medulla oblongata. Sachs collected 27 cases with 17 in six families, all in Jews.

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IV. Indiscriminate Lesions of the Spinal Cord

1. Myelitis

Myelitis is an inflammation of the cord characterized by either focal or disseminated lesions leading to softening, with associated secondary changes usually including destruction of the substance of the cord after a stage of hyperemia in which the elements are replaced by oil globules. The ganglionic cells are usually vacuolated, and show evidences of far-reaching degeneration.

The *course of the disease* is materially influenced by its *cause,* the *mode of onset* and its *distribution.*

Classification.—When the lesions are limited to the gray matter it may be characterized as *central myelitis* or *poliomyelitis.* This may be either *acute or chronic* and is separately considered among the infectious diseases (See Poliomyelitis).

When the gray and white matter are involved, it is a *diffuse* or *general myelitis;* a number of foci are found in different parts of the cord. This diffuse disease is often of syphilitic origin, or it may accompany other acute infections.

Transverse myelitis is synonymous with *compression myelitis* and depends upon compression (accident usually) following fracture of the spinal column, caries of the spine (tuberculosis), tumor—either primary or secondary—usually metastases to the membranes and vertebrae. These cases are not in reality true myelitis, but by common consent have continued to be considered in the same chapter.

Unilateral myelitis gives rise to the *Brown-Sequard symptom complex;* it may follow accident, tumor compression or disease of the substance of the cord.

In *Bulbar myelitis* the disease, either early or late, invades the medulla, causes the usual *"bulbar symptoms"* and leads to death in almost all cases.

When the process is limited to a single small area in the cord it is known as *"focal myelitis."*

All of these forms of so-called myelitis are either (a) *acute* or (b) *chronic* and for purposes of prognosis as well as diagnosis I will so consider them.

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(a) Acute Myelitis

The *majority of cases* of acute myelitis are of *secondary origin and are associated with the infections.* Among these are typhoid fever, influenza, erysipelas, gonorrhea, smallpox, pneumonia, tonsillitis, measles, cholera, diphtheria, dysentery, whooping cough and syphilis.

Traumatism including fractures and dislocations, *alcoholism* and *compression with meningitis* may also cause the disease.

Primary Causes.—Primary causes of acute myelitis include exposure to cold. It is questionable whether exposure to cold without added infection is ever a cause of myelitis. *Sexual excesses* do not cause myelitis when uncomplicated.

Prognosis.—The prognosis of all forms of acute myelitis depends upon the extent and cause of the disease. *All cases of acute myelitis present a grave prognosis.*

Traumatism (fractures and dislocations) causing transverse myelitis by compression, leading to paraplegia (sensory and motor paralysis), bladder and rectal symptoms, as well as trophic changes, including bed sores (decubitus), offer an unfavorable forecast. *The higher the lesion, the more acute the course, the greater are the dangers to life.*

Early symptoms of sepsis are always unfavorable, the condition leads to overwhelming *toxemia* from which the patient rarely rallies; if he does, it is to fall into a *subacute* or *chronic* stage in which cystitis, bed sores, and overwhelming systemic *infection* lead to *exhaustion, increasing stupor and death.*

The more extensive the paralyses, the graver the prognosis. The *acute* and *suddenly arising paraplegias* when not due to continuous compression but true myelitis, often offer a fair prognosis.

Patients with bladder and rectal paralysis rarely recover unless the cause is promptly removed.

Compression or disorganization sufficient to cause sphincter symptoms with or without decubitus, which persist during several days or weeks, lead to changes which are not likely to disappear completely under any treatment, however radical.

With the removal of the cause, after irreparable degenerative change in the cord substance which makes return of function impossible, patients may fall into a chronic stage, in which with care, life may be prolonged during long periods; the symptoms depend on the location and extent of the primary lesion.

Decubitus (bed sore) is always an evidence of either neglect or of serious and destructive myelitis. The accompanying *sepsis* drains the vitality of the patient; if under these conditions life is prolonged, he grows more and more *anemic,* shows the *evidences of chronic sepsis or pyemia.* In the terminal stage the *sensorium* is involved and the patient

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dies with all of the symptoms of *profound toxemia. The earlier the bed sore appears, the less favorable is the prognosis.*

When the *lumbar cord* is involved the *patella tendon reflex* is abolished; also the *skin reflex;* the *anesthesia* corresponds with the extent and location of the pressure. *Bladder and rectal symptoms* are also persistent.

With cervical myelitis dependent upon infection or persisting pressure from whatever cause, if the patient lives, *atrophy with paralysis of the arms* develops, also *spastic paralysis of the legs with anesthesia of the body* below the lesion, and in some cases *pupillary changes.* In these cases the development of symptoms is often sudden and with *respiratory* and *heart paralysis* (vagus) including *tachycardia* and *dyspnea,* death promptly follows.

With cervical myelitis, pneumonia, bronchitis, cystitis and *bed sores* are the most frequent causes of death.

There are occasional cases of acute myelitis in which the symptom complex is not complete but sufficient to justify the diagnosis, the cause remains unrecognized; these cases may recover under treatment and rest. It may be that in some of these there is a syphilitic fundament.

With *acute infection,* or in cases in which the cause remains unrecognized, the onset of the disease may occasionally be sudden, the symptoms develop rapidly and death may follow before the end of the fifth, at times the seventh, day.

These cases are often of the *diffuse type. Motor paralysis is prompt and ascending,* resembling Landry's disease; this type of the disease is associated with high fever.

In all forms of myelitis *irregular and intermittent fever* is likely to depend upon complications, usually decubitus, cystitis, pyelitis or pyelonephritis.

Transverse myelitis from whatever cause offers an unfavorable prognosis; the majority of these patients die of sepsis with bed sores, cystitis and anemia after varying periods of *fever* and other *constitutional symptoms.* The more favorable cases of acute myelitis are those due to the infectious diseases.

Oppenheim claims that of these, *cases secondary to gonorrhea* offer the more favorable prognosis. When the gonorrheal cases are complicated by endocarditis the prognosis is bad.

Foudroyant cases (acute hemorrhagic myelitis) with acute infections (typhoid fever, erysipelas and smallpox) lead to death within a few days.

Acute syphilitic myelitis recognized early and promptly treated offers a fair prognosis (See Syphilis, Spinal Complications).

When the symptoms of myelitis develop gradually and there is no recession of these, the prognosis is less favorable than in those cases in

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which there is sudden development of incomplete symptoms after a short prodromal period.

Neither blood examination nor the withdrawn cerebrospinal fluid offer any data of value for prognosis.

(b) Chronic Myelitis

Causes.—Most forms of chronic myelitis are of syphilitic origin, and are separately considered (See Syphilis of the Cord). There are chronic cases which develop from the acute, to which reference has been made in the preceding paragraphs.

Chronic myelitis which develops independently of other disease is so rare as to justify a strong doubt of the possibility of its existence. Most cases which are diagnosticated as chronic myelitis are due either to compression myelitis, i. e., tumor, multiple sclerosis or spinal syphilis.

Associated Diseases.—There are cases of *chronic lead poisoning* associated with symptoms of myelitis in which conditions remain unchanged during long periods.

Naturally the prognosis is unfavorable in those cases of *chronic spinal meningitis* with *chronic myelitis, caries of the spine, new growths and aneurism.*

Compression myelitis due to metastases to the spine secondary to cancer of the breast, stomach, intestines, uterus or other organs, runs a chronic course; it is among the most painful of all affections and leads to death with characteristic cachexia and exhaustion. These cases are not infrequent and at times are an early complication of breast or stomach cancer.

Myelitis which develops during pregnancy may yield to treatment. Some of these cases relapse and create the strong suspicion of multiple sclerosis. With the history of chronicity the chances of the recovery of such cases are small.

In some cases of subacute myelitis developing from the acute form of the disease, several weeks or months may lapse before the symptom complex is complete.

Death is the fate of most myelitics with symptoms of sepsis or pyemia, bed sores and cystitis, though there are a good number of cases recorded in which disseminated myelitis led to recovery.

Long periods of latency in chronic cases are not infrequent.

Cases of multiple neuritis which are associated with symptoms of myelitis occasionally recover.

In both acute and chronic myelitis the *general condition* of the patient and *possible complications* are powerful factors in prognosis.

The *aged* and *enfeebled* offer a uniformly bad prognosis.

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2. Multiple Sclerosis of the Brain and Spinal Cord

(*Disseminated Nodular Sclerosis, Sclerosis en Placques*)

Characterization.—Multiple sclerosis of the brain and spinal cord is as a rule a *chronic progressive disseminated disease* of *uncertain origin,* characterized by the development of numerous indiscriminately located sclerotic nodules, easily recognized by the unaided eye. The process is degenerative and productive.

The disease presents the anatomic characteristics of *chronic interstitial myelitis.*

The nodules or placques are of a gray color, translucent, resistant and hard.

Course of the Disease.—When the disease is fully developed the "islands" are scattered throughout the cord and brain, and the peripheral nerves may also show "sclerosis." The placques or nodules are distinctly outlined and microscopically the neuroglia is found reticulated and fibrillated.

In the brain, the *seats of predilection* are the pons, the centrum ovale, the walls of the lateral ventricles, the corpus callosum, the gray matter of the central ganglia and the cortex. The cord is involved at various levels.

The *medulla oblongata* often escapes. In the cord, the *pyramidal tract* is the favorite seat of sclerosis (white fibers) but as Charcot pointed out years ago, *large numbers of axis cylinders escape, thus preventing complete paralysis.*

Secondary degeneration is rarely present—never extensive.

With the advance of the disease, the *vessel walls are thickened* but the placques show no tendency to contract. There is, according to Strümpell, a marked similarity to *central gliosis* and he considers the process one of "gliomatous degeneration." The possibility of regeneration of the axis cylinder accounts for the improvement in some cases after varying periods.

Age.—The majority of my cases were found between the ages of 20 and 30 (rarely after 45). The sexes are equally affected. I have seen no case occurring during early childhood. Oppenheim demonstrated the presence of congenital stigmata in the few cases in early life which he has seen, and Eichhorst reports a child 8 months of age with marked sclerosis *en placques* in which the mother was also suffering from the disease.

It may be safely assumed that when the disease is found fully developed between the tenth and fifteenth year of life that it has already existed during a number of years. In such cases the advance is always so

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slow as to remain almost unnoticed until the leading features of the fully developed disseminated deposits are characteristic.

Cause.—The cause of multiple sclerosis is uncertain. The majority of my cases have followed acute and grave infections; of these typhoid fever was the most frequent. Among the remaining infections which have preceded multiple sclerosis are diphtheria, influenza, smallpox, scarlet fever, measles and malaria. Syphilis is not considered to be a frequent cause of multiple sclerosis.

Spiller and Woods (quoted by Oppenheim) have reported a number of cases which they believe rest upon a syphilitic fundament. Most authorities deny the association of syphilis as a causative factor.

There are a number of cases in medical literature which followed childbirth.

Strümpell believes that *traumatism* is a comparatively frequent cause of the disease and calls attention to the importance of this fact in "accident practice." *I have never in my experience seen a single case of multiple sclerosis after injury of any kind.*

In the large majority of insular scleroses the cause remains unrecognized.

Whatever the cause in the individual case, it may be safely concluded that it does not materially influence the forecast of the fully developed disease.

The disease is more frequent in England than on the Continent of Europe, where it is oftener found than in the United States. Unquestionably many of the atypical types ("formes frustes") have been incorrectly diagnosticated in our country. The more thorough knowledge of the clinical history of these cases and the better knowledge of its pathology are already leading to more frequent and correct diagnosis.

Symptoms.—The leading features of the disease—intentions tremor, muscular rigidity, nystagmus, exaggerated tendon reflexes (Babinski phenomenon), scanning speech, vertigo, often optic neuritis, spastic and paretic gait, final muscular weakness—once established, usually remain, and while there may be *periods of latency* and at times *apparent recessions*, the lesions which cause the symptoms are not often overcome.

I have never seen disappearance of symptoms in typical cases in which with *loss of abdominal and cremaster reflexes* there was nystagmus, scanning speech, and exalted knee reflex.

The typical symptoms above mentioned may follow a complex referable to the *optic nerve* with *nystagmus and but slight change in speech* after months or years. After these periods of latency the onward march is usually continuous but slow.

Optic neuritis is only partial as a rule and rarely leads to complete optic atrophy. In most of my cases optic change was among the early lesions; it may precede by a number of years most of the other usual

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symptoms, as Frank and Windmuller have also demonstrated. There is in occasional cases marked improvement of the ocular symptoms or periods of latency or remission.

Uhthoff and many observers have called attention to the frequency of extreme *pallor of the temporal half of the optic disk* in fully developed multiple sclerosis. The *prognosis so far as sight* is concerned in these cases is not bad, for *complete blindness as a complication is exceedingly rare* and the *anemia* may persist without causing subjective symptoms. In some cases there is *contraction of the visual field,* and in occasional cases blindness of one eye has continued during varying periods, after which it disappeared. The pupillary changes rarely lead to loss of the light reflex.

Multiple sclerosis in which the early symptoms are referable to the eye progress slowly, are likely to have long periods of latency, and are among the most chronic of all cases—at times the history includes several decades of symptoms.

Papillitis is often evanescent in the midst of other symptoms of insular sclerosis.

There are cases which begin with marked *ataxia,* are associated with *ocular symptoms* and are also exceedingly chronic.

The *bulbar* or *bulbopontine complex* may characterize some cases early and lead to erroneous diagnosis and prognosis, or after years of typical symptoms *bulbar lesions* develop and lead to death.

Scanning speech may persist during years in the presence of other evidences of sclerosis without influencing the course of the disease. Scanning speech, which is slow and decided with marked spastic paraplegia, nystagmus, intentions tremor and optic neuritis, is *evidence of advanced and far-reaching dissemination* and in most cases there is no decided improvement of any of the symptoms, though the diseases may remain stationary during long periods without threatening life.

There are cases in which *apoplectiform seizures* occur, and after a few hours or days the associated hemiplegia gradually disappears. These apoplectiform attacks are often associated with hyperpyrexia, rapid pulse, and respiratory symptoms. Rapid progression of the disease often follows the attack.

Once developed, *epileptiform attacks* are likely to recur; these are not often true epilepsy, though the latter may in rare cases complicate multiple sclerosis. No treatment influences the explosive seizures.

Staggering, headache and *vertigo* are persistent and often prove a serious handicap (cerebellar type).

When the disease advances to the stage in which there are evidences of *mental deterioration,* improvement is not to be expected.

Impulsive laughing and crying have in my experience been associated with the more advanced cases in which the mental state is more or less

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disturbed, or in those with hysterical tendencies—cases which are progressive as a rule.

Paralysis of ocular muscles occasionally disappears; as a rule it is persistent.

There are a number of cases recorded in which *ophthalmoplegia* which is not a frequent complication, disappeared (Oppenheim).

Diagnosis and Prognosis.—*The behavior of the cutaneous reflexes in contradistinction to the tendon reflexes is of great importance for diagnosis and prognosis.*

The *cutaneous reflexes are usually markedly* reduced, and the absence of the abdominal and cremaster reflexes is one of the early and most important features of the disease to which Strümpell and E. Muller have called attention (Strümpell and Oppenheim).

When with suspicious symptoms of *incipient insular sclerosis the abdominal reflex is abolished,* the diagnosis may be made with great certainty and the prognosis accordingly given.

Persisting incontinence of urine and rectal disturbances are evidences of advanced sclerosis. *Transitory sphincter symptoms* are not unusual during the early stage of the disease and are not of serious importance.

Lumbar puncture offers no data for prognosis. In a few cases globulin (Nonne reaction, Phase 1) will be found, and lymphocytosis is not unusual.

In framing the diagnosis and prognosis of multiple sclerosis, cautious inquiry into the history of cases with fully developed symptoms which may appear to have been developed within a limited period, will prove that the disease has in reality existed during several years; that it is insidious and as a rule, there are periods of latency, often of remission.

The partial motor insufficiencies of the early stage of multiple sclerosis, *marked weakness* in some cases, disappear as a rule, and do not influence the prognosis materially.

It should be remembered that temporary improvement, remission, repeated relapse and chronicity are characteristic of the disease.

The *increase of symptoms in cycles,* in a measure, accounts for the duration.

Only rarely does the disease progress to a fatal termination rapidly; such progression as already mentioned, is most likely to follow apoplectiform attacks.

Death may occur early in the exceptional cases in which the medulla oblongata is invaded or it may promptly follow in chronic cases when such complication is added.

Bramwell reports four cases of multiple sclerosis which recovered; Maas also believes that recovery is among the possibilities; Oppenheim reports a cure after facial erysipelas, while Charcot and Marie many years ago insisted that the prognosis was not absolutely unfavorable in all cases.

Atypical Types of Multiple Sclerosis.—Atypical types of mul-

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tiple sclerosis are numerous; each offers features which materially influence prognosis.

There are cases which are *latent during long periods* in which the *clinical features are so incomplete as to remain unrecognized* in which *apoplectiform seizures arise suddenly, are followed by remission, later by epileptiform attacks and early death.* In these cases the lesions of the fully developed disease are found post mortem.

Cases with symptoms of spastic spinal paralysis are as a rule chronic and are likely to be complicated by optic atrophy, but do not often lead to blindness.

Spinal hemiparesis (Oppenheim) and *cerebral hemiplegia of sclerotic origin* may develop slowly; tremor persists in one-half of the body. These cases run a protracted course.

I have already mentioned in preceding paragraphs of this chapter the course of the disease with *bulbar involvement. The rare cases of acute and promptly fatal insular sclerosis* are likely to be of this type when not apoplectiform.

There are cases of multiple sclerosis which closely resemble *transverse myelitis.* In these cases there are *cerebral lesions* so limited as to cause but few symptoms. These cases also run a chronic course, usually show *ocular changes* but are not completely incapacitated until the late stage of the disease.

Cases with *ataxic symptoms in the ascendency* in which there are loss of patella tendon reflex, sensory disturbances, including crises and the Argyll-Robertson pupil, include besides the usual lesions of multiple sclerosis, degeneration of the posterior columns. These case progress slowly and finally lead to a paralytic stage in which bed sores, cystitis and sepsis precede death. In the *sacral type,* bladder incontinence is present early; there is flaccid paralysis of the lower extremities and loss of patella tendon reflex. These cases progress slowly.

The majority of atypical cases are *progressive* though stationary periods and remissions with improvement of individual symptoms are frequent.

Whatever the type of multiple sclerosis, the disease justifies only the gravest prognosis in spite of the few cases mentioned in which recovery is supposed to have been complete. *The fate of the sclerotic* if he does not yield to intercurrent disease is *chronic invalidism* which includes months and years during which he is bedridden with many complications, including urinary incontinence, cystitis, bed sores, and often mental lethargy.

Great caution in prognosis is necessary because of the long periods of latency and remissions which characterize the disease, and which may lead the enthusiastic and inexperienced to favorable but wrong conclusions.

The *favorable forecast concerning sight* mentioned in this chapter is justified, for in a long experience, blindness has never complicated my cases.

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It is not uncommon to find cases which have lived over twenty years, and I number among my material one man who lived forty years with well marked symptoms of the disease, incapacitated during thirty years—over twenty years of which he was practically helpless in bed or in a roller chair. He died of pneumonia.

COMPLICATIONS.—Most cases of insular sclerosis yield to complications.

Pneumonia is a frequent cause of death, particularly during the last stage of the disease.

Septic and pyemic conditions are provoked by bed sores, cystitis, pyelonephritis and other complications; there may be weeks of symptoms before death; rarely does septicemia end acutely.

Locomotor ataxia, paralysis agitans, epilepsy and syringomyelia have occasionally developed.

TUBERCULOSIS kills a small proportion of multiple sclerotics.

3. *Pseudomultiple Sclerosis*
(*Westphal-Strümpell*)

Westphal and Strümpell have reported cases which lead to death, with many of the symptoms of multiple sclerosis but without characteristic discoverable lesions, in which the diagnosis is exceedingly difficult and which are known as *pseudomultiple sclerosis.*

Symptoms.—The leading features are the early development of psychic disturbances, violent emotions, outbursts of anger and maniacal attacks with the persistence of oscillatory tremor, rigidity of facial expression without ataxia, but with persistence of the deep reflexes and spasticity. The optic nerve is not involved.

For prognosis and diagnosis the *early appearance of dementia* with other symptoms of multiple sclerosis and the *slow oscillatory tremor* will prove valuable, besides the fact that *the tremor, in contradistinction to the intentions tremor of multiple sclerosis persists during repose.* Nystagmus does not develop.

For the thorough study of the *clinical features* of pseudosclerosis, the reader is referred to the papers of Westphal and Strümpell, to which reference is here made and to the literature which is included in Oppenheim's treatment of the subject.

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4. *Abscess of the Spinal Cord*

Abscess of the spinal cord occasionally develops; it is always secondary to coexisting lesions which are usually due to traumatism or infection. It is therefore metastatic as a rule.

Associated Symptoms.—The cases recorded have followed distant pus deposits in the prostate, purulent cystitis and bronchitis, gonorrhea, and purulent meningitis, and have led to a fatal termination with all of the symptoms of meningitis, which usually preceded paralyses, motor and sensory, and trophic disturbances (bed sores).

Course of the Disease.—The *rapid advance* of the disease after the initial symptoms of spinal meningitis is characteristic; the *paraplegia* is promptly developed with the other features of indiscriminate disease of the cord including in some cases ascending symptoms, anesthesias and sphincter involvement.

The *blood picture* of the associated infection and cultural methods aid in diagnosis and prognosis.

The disease, as a rule, runs an *acute course*, terminating in death within the first seven days. Only rarely is the course of the disease protracted after the metastases to the cord, though such a history is not impossible.

5. *Syringomyelia*

(*Gliosis of the Spinal Cord*)

Symptoms.—Syringomyelia is characterized by the formation of abnormal cavities in the spinal cord, often of congenital origin, either a dilatation of the central canal of the cord (*hydromyelus*) or *central gliosis and the secondary formation of cavities*—true syringomyelia.

Schlesinger, whose article should be consulted for full clinical data, found that the majority of cases are exceedingly chronic, usually begin before the thirtieth year, and after that men suffer three times as often as women.

While the majority of cases rest upon a *congenital basis*, there are evidences which justify the conclusion that *traumatism in the predisposed* may prove an exciting factor.

Slight congenital (*hydromyelus*) *dilatations of the central canal* are often found post mortem without having caused symptoms during life.

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Congenital hydromyelus may follow the faulty closure of one of the divisions of the central canal of the cord (Herter).

In true syringomyelia there is a "disintegration of gliomatous formation which usualy originates in embryonal tissue about the central canal."

Pressure from tumors may cause hydromyelus and offers data for diagnosis and prognosis.

Classification.—True syringomyelia may cause *dilatations* in any part of the cord besides the central canal, in one or both anterior or posterior gray horns, by predilection in the cervical spine. It should be considered of *congenital and neoplastic origin with subsequent disorganization of the new tissue, more particularly in the gray matter of the cord and the consecutive formation of cavities.*

The disease does not lead to lesions of the *peripheral nerves* except in rare instances. Oppenheim reports such involvement but says that it is of no importance for symptomatology, hence of no prognostic value.

The course of syringomyelia is slowly progressive and characteristic. There is a *trio of typical symptoms* which deserves consideration:

1. Muscular atrophy
2. Sensory disturbances
3. Trophic symptoms.

1. Muscular Atrophy.—When there are symptoms of muscular atrophy showing involvement of the cervical spine of the Aran-Duchenne type of progressive muscular atrophy with fibrillary contraction and reaction of degeneration, there are usually sensory symptoms as well. The *triceps reflex* is soon lost, the progression to the muscles of the face and lower extremities is not usual. The *atrophy may remain unchanged during long periods* and the *reaction of degeneration may be limited to single muscles or parts of the larger muscles* during indefinite periods. The reaction of degeneration is not always present.

With the advance of the process and involvement of the ciliospinal center, myosis, ptosis and enophthalmus may develop, while one-sided atrophy of the tongue, facial paresis and partial pneumogastric paralysis may also complicate some cases—all depending upon the location and extent of the gliosis.

Unilateral paralysis of the vocal cords, demonstrated by laryngoscopic examination will often prove of great diagnostic and prognostic value.

2. Sensory Disturbances.—Sensory symptoms of syringomyelia are *characteristic;* once present they persist and remain uninfluenced by treatment.

Among the *earliest symptoms* are often complete or partial loss of sensation of heat, cold, and analgesia (loss of the pain sense) without interference with the tactile sense. The last case included in my material covered a history of over three decades, during which these sensory

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symptoms persisted and in which acromegaly with other complications developed without marked muscular atrophy but with the Morvan syndrome (Elsner).

In these cases it is often possible for patients to continue at occupations in which they are protected from injuries due to burns and other wounds.

The *dissociated sensory disturbance* depends upon the seat of the atrophy. With sensory symptoms of the face there is usually atrophy. As a rule atrophy and the characteristic sensory disturbances are coexistent.

Tactile anesthesia, disturbance of the muscle and the pressure senses are evidences of advanced disease. These sensory disturbances are never early manifestations of syringomyelia; they are usually absent throughout the disease, and when present denote advance to the white posterior columns.

3. Trophic Symptoms.—*Morvan's disease,* to which I have referred in connection with the sensory disturbances, is a variety of syringomyelia in which trophic changes are in the ascendency, including recurring whitlows, often multiple, with muscular atrophy, analgesia and paresis. Both upper and lower extremities may be involved. The prognosis of these cases is unfavorable, the course chronic.

There are cases of syringomyelia in which *trophic symptoms* are prominent from the beginning, and continue so throughout the entire course of the disease.

Necrobiotic processes and *vesicles* are often recurrent. *Ulcerative destruction* does not, as a rule, repair easily. *Repeated injury, burns and other wounds of tissues* without normal resistance or vitality, open avenues for infection; in some cases there are almost continuous surface lesions. *Perforating ulcers* may lead to deep destruction of tissue.

Trophic disturbances of the nails, overgrowths of the skin, edematous swellings and bone lesions remain uninfluenced; they are likely to increase or become multiple.

I have seen several cases with *Raynaud's symmetrical gangrene* entirely uninfluenced by treatment.

The *anomalies of perspiration, anidrosis, hyperidrosis, hemidrosis* may develop early or late.

The cardinal symptoms and course of the disease are easily understood if we associate the *analgesia and thermanesthesia with changes in the posterior horns, the muscular atrophy with the anterior horns, the trophic vasomotor disturbance with the gray matter* and the *spastic paralysis with the lateral columns. Tabetic ataxic symptoms with tactile disturbance show involvement of the posterior column.*

Spontaneous fracture and *dislocations,* also *arthropathies,* are trophic

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changes of the advance stages of the disease. The latter complicate from 8 to 12 per cent of all cases.

Spinal curvature frequently develops; it is also found in the younger subjects; it develops gradually in adults and in the advanced stage leads to marked deformity.

The *atrophy* and *paresis of the spinal muscles*, often one-sided, is a cause of *scoliosis*, but as Strümpell says, does not explain all cases; the unexplained, he says, are "an expression of the abnormal conditions of development and growth in the vicinity of the spinal cord."

Cases which develop *bulbar symptoms* are usually associated with *hemiatrophy of the tongue* and are often complicated by *pneumonia* or other acute infections, which shorten the duration materially, or the progression may be rapid after the beginning of the central invasion. *Bulbar symptoms may develop suddenly after years of chronicity.*

Diabetes mellitus developing in young subjects with syringomyelia leads to prompt emaciation and death, with symptoms of *acidosis*. Such cases are but *little influenced* by diet or other treatment.

Syringomyelia occasionally complicates *cervical hypertrophic pachymeningitis* (Oppenheim, Holmes-Kennedy, Phillipe-Oberthür). The course of these cases is exceedingly chronic. In the later stages the lower extremities are involved; the patient becomes bedridden, with in the end, most of the complications of the typical cases including cystitis, bedsores and sepsis.

Tabes dorsalis and paresis may be complicated by syringomyelia with optic atrophy and the Argyll-Robertson pupil.

Pseudotabetic gliosis described by Oppenheim is progressive and denotes posterior invasion resembling, in its symptomatology, true locomotor ataxia. As the disease advances there are evidences in symptoms of dissemination of the process in various parts of the cord.

Psychic disturbances are not among the early symptoms; when present they complicate the terminal stage.

Caries of the spine when complicating syringomyelia leads to a febrile state in some cases with rapid pulse and evidences of toxemia, besides the usual trio of symptoms due to indiscriminate disease of the cord.

The development of keloid tissue, ankylosis of small joints, Dupytren contractures and necrosis of bone—usually of the terminal phalanges of the fingers—do not as a rule influence the prognosis materially so far as life is concerned.

The addition of symptoms referable to the lower extremities, spastic paraplegia with cystitis or rectal disturbances denotes far reaching gliosis and is unfavorable. In some cases associated with spastic conditions early (amyotrophic disease), sensation may remain normal during many years.

While syringomyelia is a disease which may continue with but slight

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progression during long years, it remains uninfluenced by treatment. It is a disease which, as already suggested, is dependent upon congenital anomalies which lead to early and often unrecognized symptoms, making the duration of the disease one of the longest of all diseases of the central nervous system. In one of my cases the history covers almost fifty years and the patient is still alive.

The *average duration* is between fifteen and twenty years. With *bulbar invasion* it is considerably shorter.

As a rule death is not directly due to the disease but to some complication.

Cystitis, bed sores, pyelonephritis, sepsis following burns and injuries, pneumonia and occasionally tuberculosis, are among the *more direct causes of death.*

The clinician is not to be deluded by apparent *remissions* and *periods of latency*, for it will be found that *once established the disease remains and ultimately leads to death, either directly or indirectly.*

It is often surprising to note how long many of these patients are able to continue their occupations with clear minds.

The association of *syringomyelia* with *acromegaly* is usually accompanied with great mental depression. In one of my cases there was strong suicidal tendency.

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6. Tumors of the Spinal Cord

Tumors of the spinal cord, with the exception of gumma, are uninfluenced by medical treatment. Unless treated surgically the prognosis is absolutely bad.

Primary growths of the cord are comparatively speaking, exceedingly rare. Pathologic evidence argues against the occurrence of intravertebral growths of primary origin, and in favor of the preponderance of secondary deposits which are either extramedullary or intramedullary.

Classification.—The classification of Bruns divides the growths of the cord into: (I) *extramedullary tumors:* growths which originate in tissues around the cord and invade its substance secondarily by growth with extension; and (II) *intramedullary growths:* growths which originate in

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the substance of the cord; these are oftener primary than are the extramedullary tumors.

I. Extramedullary Tumors

(a) Vertebral tumors. These originate in the vertebrae or in the surrounding soft tissues.

(b) Intravertebral tumors. These growths originate in the spinal membrane, and they may be either (1) Extradural or (2) intradural.

Extradural tumors originate in the periosteum of the vertebral canal, the external surface of the dura, or in the extradural tissue (fat, etc.).

Intradural tumors originate from the inner surface of the dura, the arachnoid, the ligamentum denticulatum, the nerve roots or the pia mater.

II. Intramedullary Tumors

Growths which originate in the substance of the cord—in the medullary substance—are intramedullary.

I. Extramedullary Tumors

The majority of spinal growths are intravertebral—either extra- or intradural, oftener extradural. Jacobsohn reports the proportion of extra- to intramedullary spinal growths as 3:1. Further he reports 6 cases of spinal tumors in 9,626 cases of diseases of the nervous system treated at the Moabit Hospital in ten years.

Schlesinger reports 147 tumors of the cord in 35,000 autopsies. In 151 tumors of the brain and cord of 6,540 tumors, Starr found brain tumors thirteen times more frequent than those of the cord.

In 5,115 cases of internal diseases I found 9 spinal tumors.

"Metastasis in the central nervous system secondary to carcinoma elsewhere in the body may assume many forms. It may occur as a multiple carcinomatosis which may or may not be a part of a general carcinomatous process elsewhere."

"There may be only a few cancer nodules within the central nervous system, or the process may involve the brain or cord and the meninges extensively, or the meninges alone. The meningeal infiltration may be either diffuse, as a carcinomatous meningitis, like the sarcomatous meningitis, or may be in the form of multiple tumors. Metastasis to the substance of the cord is exceedingly rare and is nearly always from the periphery of the cord. Metastasis to the vertebrae is most common" (Spiller and Weisenberg).

The metastases of the cord and spine which interest the internist most are due to cancer of the breast, stomach, and intestines.

The study of the relative frequency of metastasis to the spine from

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breast and stomach cancer proves the former to be twice as frequent as the latter.

Schlesinger's statistics are conclusive on this point. Thus, in 54 cases with metastases to the vertebrae and spinal membranes there were cancers of the breast, in 10 cases; esophagus, in 9 cases; thyroid in 9 cases; uterus in 6 cases; bronchus, in 5 cases; stomach, in 4 cases; prostate, in 3 cases; gall-bladder, in 2 cases; ovary, in 1 case; sigmoid flexure, in 1 case; rectum, in 1 case; kidney, in 1 case; adrenal, in 1 case; pancreas, in 1 case; not specified, in 1 case.

The metastases to the nervous system, particularly, the extra- and intradural growths, are oftener due to breast cancer than to other primary growths. It is not uncommon to find advanced symptoms of pressure due to metastases to the dura or vertebrae giving rise to symptoms before the diagnosis of breast cancer has been made. Thus, in a case of transverse myelitis clearly due to compression, the patient had never mentioned the presence of scirrhus of both breasts. The masses were accidentally discovered during the physical examination of the advanced case in which myelitis alone had been suspected.

Long periods of latency of breast, stomach, intestinal, prostatic and other cancer do not preclude the possibility of extensive and increasing metastases to distant organs—spine, brain and peripheral nerves.

There may be palpable tumors of the stomach, breast, intestines or distant organs without marked symptoms in which the prognosis of the primary growth is not threatening, but in which early metastasis to the cord or spine, occasionally to the peripheral nerves or brain, may lead to death or may during considerable periods overshadow entirely the symptoms of the primary growth, because of the intense suffering and paralysis due to compression and infiltration.

The possibility of long periods of improvement in the visceral carcinomata due to periods of latency which positively exist, have not been generally recognized by the profession, and it is during these periods that metastases to distant parts may follow. A small cancer nodule in the stomach or intestines may exist without local symptoms, and may remain unrecognized; painful metastasis to the spine or to the membranes of the cord may offer the first evidence of malignant disease. Cases of stomach cancer without symptoms in which metastases to the nervous system are present may exist, in which, as in dogs, after gastrectomy the intestinal tract soon learns to compensate for the loss of the stomach function. It is not uncommon, because of a sufficient remnant of gastric follicles and functionating mucosa, to find the characteristic features of cancer of the stomach absent during comparatively long periods. This condition does not preclude the possibility of metastasis to distant organs.

The majority of tumors originating in the meningeal coverings of the cord are benign and of slow growth. Hence symptoms of compression

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of the substance of the cord are long postponed, and the recognition of the nature of the process during the early period when neuralgic pains are among the leading manifestations with prompt localization and operation, will lead to the most satisfactory results.

Correct interpretation of *neuralgia*, persisting, and rebellious to treatment, will often lead to the accurate diagnosis; rational and radical treatment will be rewarded with increasing success as experience grows.

Sciatic pain, one-sided, uninfluenced during a reasonable period, which finally becomes double and continuously rebellious, is often an expression of compression due to tumor; the prognosis depends on the nature of the growth, its extent and location. It will be found that a few (comparatively speaking) of these growths will prove to be operable.

In prognosis it is always wise to consider sensory symptoms, long localized and persistently uninfluenced by treatment, referable to the cord, to be due to compression, either to inflammatory, tuberculous, malignant or non-malignant disease. This is particularly true of sciatic pains.

Symptoms of irritation, spasms, convulsive seizures, associated with other focal symptoms and persistent pain which are suggestive of compression, often continue during many months without rapid advance of the disease.

There are both rapidly and slowly growing tumors of the cord and spine in which the absence of sensory symptoms (pain), spasm and focal symptoms, are frequent, but progression is nevertheless positive.

Many tumors of the cord are benign; some are only semimalignant.

Cachexia even with the malignant metastases may be absent during long periods; the absence of cachexia with positive symptoms of metastasis, following the removal of distant malignant growths, does not argue against the same histologic build of the secondary growth.

The prognosis of these metastatic growths without cachexia is uniformly unfavorable; the course may be chronic.

The behavior of the tendon reflexes with spinal growths as they begin to compres the cord, is quite characteristic and its thorough understanding in operable cases may lead to the necessary early diagnosis.

Often *exaggerated reflexes are among the earliest symptoms*—patella tendon reflex, ankle clonus and Babinski phenomena are prominent—*particularly in the limbs in which paralysis is most advanced.*

The abdominal reflexes are absent or weakened.

Brown-Sequard paralysis makes localization easy.

The cautious outlining of the level of sensory symptoms (anesthesia, hyperesthesia, etc.) in most cases makes it possible to localize the growth, often after a long period during which extension has been gradual.

Bladder and rectal paralyses are evidences, as a rule, of *compression;* they are usually found in advanced cases and are unfavorable symptoms. The presence of *bed sores* in such cases leads to overpowering sepsis.

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The usual seat of tumors springing from the meninges is in the dorsal region.

Cervical invasion very often leads to spastic paralysis. Finkelnburg calls attention to development of flaccid degenerative paralysis of the arm muscles after a period of neuralgic pains; the *invasion of the dorsal cord* causes changes in the adjacent sympathetic and the development of pupillary symptoms.

The prognosis of extramedullary growths of the dorsal region for surgical interference is more favorable than is that of cervical lumbar or caudal invasion. This is equally true of extra- and intramedullary growths.

Gowers, Horsley and Oppenheim contend that intradural growths are almost always operable; they grow slowly, are likely to be benign and their attachment to the cord itself is easily overcome.

"Out of twenty-four laminectomies performed in the Neurological Institute during the year ended Nov. 30, 1913, there was only one death, and this patient died after a second-stage laminectomy for a suspected tumor of the cervical cord, a highly precarious region. Considering this slight mortality, I feel little hesitation in recommending exploratory laminectomies by skillful operators in cases in which spinal cord tumor may exist, especially in view of the fact, now established, that painlessness does not deny such existence" (Bailey).

II. Intramedullary Growths

The increasing success following the surgical removal of the intramedullary tumors is encouraging and has, since the radical statements made by Gowers and Horsley, encouraged the clinician to the belief that these growths are often operable and that a successful issue may be expected in a large proportion of cases if the growth is removed early, before destruction of the cord substance.

In many, the growth cannot be diagnosticated until *compression symptoms and disorganization* are in evidence.

Another fact which influences the early diagnosis of intramedullary growths is the *absence of neuralgic pains* during the early stages in a large proportion of cases.

Schlesinger's statistics prove the great prognostic significance of the preceding statement for they show that almost *one-third of all tumors of the cord are within the medullary substance* (of 302 tumors of the cord, 125 were intramedullary). These include sarcoma, tubercle nodules, gumma, lipoma, cysticercus, neuroma, cholesteatoma, myxoma, teratoma, adenoma and endothelioma.

Elsberg says "many of these intramedullary growths infiltrate the cord substance and increase in size by extending upward and downward,

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but some enlarge in their transverse diameter, are encapsulated and of small size." The more favorable growths for operation are those which are encapsulated and of small size.

Gowers, whose experience cannot be ignored in our consideration of the forecast of intramedullary growths, calls attention to the tendency of "these tumors, in some cases to blend with the substance of the cord."

Infiltrating disease is less favorable for successful surgical relief than are those cases in which the "tumor is sharply limited."

Intramedullary tumors may, as Schlesinger has demonstrated, expand in such a way as to make these appear to be of extramedullary origin.

The encouraging experiences of Elsberg and others including Bruns, Allen Starr, Cushing, Bailey and Beer as well as Oppenheim, justify the unqualified statement of Elsberg that localized growths of the cord substance must not be considered as inoperable. "They should be attacked by the neurological surgeon as readily as subcortical tumors of the brain. The results should be at least as good as those obtained in subcortical intracranial growths."

It will often be impossible to differentiate the extra- and intramedullary growths, so closely may the symptoms parallel each other, but it may be assumed that a long period of neuralgic pains favors the extramedullary origin of the growth and in these cases, as already suggested, the secondary nature of the disease must be considered in prognosis in spite of great chronicity. *Years of symptoms are not uncommon particularly with breast cancer.*

The usual posterior and lateral location of tumors of the cord adds to the success of early surgical interference.

Starr reports in a series of 58 cases of tumor of the cord operated, that it was possible in all but 3 to remove the growths. These included 16 completely successful and 10 partially successful. In all of these cases the prognosis depends upon the amount of compression and destruction of the cord. Degenerative changes cannot be overcome. "The importance of an early diagnosis of these tumors is emphasized by the fact that most of them can be successfully removed if taken in time, and the fatality, which otherwise attends them, arrested" (Church and Peterson).

Putnam and Warren found that 70 per cent of recorded cases were operable, and of 33 operated cases one-half resulted successfully. Stursberg in his tabulated cases reports 32.2 per cent of cures.

In some cases life is saved but a remnant of spastic paraplegia persists. Naturally multiple are less favorable than are the single growths. Schlesinger's statistics of 400 tumors included 273 single and 127 multiple growths.

Sarcoma of the cord is of rapid growth, is likely to involve the membrane and the posterior surface of the cord, and does not lead to rapid destruction of the cord substance; it is therefore favorable for early

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operation. The ease with which sarcoma can be stripped from its resting place is a favorable fact. The growth is not likely to be encapsulated.

Infiltration is characteristic of some spinal sarcomata, the effect of which is rapidly destructive to the substance of the cord. Such behavior is the exception rather than the rule.

Multiple sarcoma of the spine offers scant, practically no chance of recovery; it is not common in such cases to find multiple growths springing from the cerebral dura and the brain at the same time.

Carcinoma of the cord offers an unfavorable prognosis; it is always secondary, more frequently found in woman (70 to 80 per cent of all cases) and is usually metastatic.

Tubercle of the cord and brain is separately considered (tuberculosis, etc.). Starr reports a case in which a single tubercle nodule was easily removed from the cord by McBurney. The patient developed general tuberculosis and spinal meningitis two months after the operation.

I have had no experience with *echinococcus* and *cysticercus cysts.* Those described in monographs and textbooks have shown rapid growth and evidences of *compression myelitis.* There is no reason why operation for growths of echinococcus origin should not be followed by the same results as have been mentioned in connection with the operation for other spinal tumors—non-malignant.

The *fibromata, psammoma, fatty growths, myxoma,* and *osteoma* offer a good prognosis for surgical treatment.

Glioma always offers an unfavorable prognosis, for it grows rapidly and its dissemination with infiltration is far-reaching.

Multiple neuromata of the cord, brain and peripheral nerves may exist together; the prognosis so far as removal of the growths is concerned, is bad. These patients may live during long periods and may die of intercurrent disease.

To determine whether a tumor of the cord is primary or secondary may in exceptional cases require a varying period of observation and, in puzzling cases, always demands thorough search of all possible sources for the primary disease.

The rectum, uterus and prostate as well as the intestines, stomach and breast supply metastases in some of these puzzling cases and should be suspected. The possibility of bronchial or pulmonary growths should not be ignored.

The growth of the spinal tumor in its bony, non-yielding canal must of necessity cause compression in most cases; hence to save these patients and change the prognosis, the *early pains* require correct interpretation. In cases of single, non-infiltrating primary tumors, cautious observation should lead to early diagnosis and surgical treatment in an increasing number of cases; as the surgeon improves his technic and his experience grows, the prognosis will improve. *Metastases* however, wherever found,

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in the membranes or substances of the cord, offer only the gravest prognosis.

Secondary growths in the cord and spine are as a rule chronic, and the history covers a period of from eight months to several years in most cases. Cases have been reported in which patients lived so long as six, eight and even ten years. It is often surprising to note how long patients may live with metastases to the vertebrae, spinal meninges and cord. I include cases which lived from three to five years after the diagnosis was made.

Cases in which there are early manifestations of complete *transverse myelitis* from extradural growths may run a course shorter than the average.

Cases of *metastasis to the spine and cord* following the surgical removal of breast cancer have in my experience averaged between eighteen months and three years after the beginning of continuous symptoms.

Spinal gliomatosis usually runs a rapid course. In these cases the infiltration is not limited to the cord, and before death there are evidences of cerebral invasion.

Glioma, it must be remembered, is rarely single; it is usually diffuse and its infiltration is far-reaching.

In almost all cases of tumor which involve the cord *when death results, it follows a period of septic symptoms in which there are evidences of ascending genito-urinary invasion, often with bed sores and extreme emaciation.*

Compression myelitis fully established with disorganization resulting from tumor, the growths of large size, infiltrating disease, multiple growths, carcinoma, metastases, glioma, all inoperable cases, offer only the gloomiest prognoses and are among the most painful of all diseases.

The *early removal of growths of limited size*—non-malignant—offers the most favorable prognosis of all operable growths.

It is unwise, in spite of the encouraging reports of surgeons and brilliant results in individual cases to give an unguarded prognosis in any case of tumor of the cord or vertebrae, wherever located.

The relation of trauma to tumors of the cord is of considerable importance, and we quote from the splendid article of Bailey as follows:

"There are a great many instances in which injury to the back, in a previously healthy person, has been followed in the course of a few months by characteristic appearances of spinal cord tumor, and in many of these cases operation has been done. The occurrence of pain in such cases is interesting, for at the time of the injury to the back there is immediate pain at the point of injury, and this pain does not entirely disappear, but remains until finally it develops into the pain of a spinal cord tumor."

X-Ray Examination.—The Röntgen rays may prove of great assist-

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ance in vertebral and extramedullary growths in localizing bony metastasis, and may thus prove of early prognostic as well as diagnostic value.

X-ray examination fails to give satisfactory results in tumors of the cord itself.

Lumbar Puncture.—*Marked increase of intraspinal pressure* with tumor is evidence of compression, and with corresponding *increase of albumin* in the fluid and *globulin* (Phase 1, Reaction of Nonne), and a *low lymphocytic content or entire absence of lymphocytes, the prognosis is unfavorable.*

Plaut reports that hemorrhages have at times been found in the tissue about the tumor after lumbar puncture, due to the sudden lowering of pressure by the withdrawal of fluid.

Klieneberger, Kindborg, and others including Quincke, report a yellow color of the spinal fluid in cases of tumor of the cord due to the presence of blood coloring matter. These cases are ominous and are usually far advanced. In exceptional cases the results of lumbar puncture added to the thoroughly digested clinical history will prove of considerable prognostic value; the data derived from the examination of the fluid *alone,* ought not to be relied upon.

Tumors of the conus and cauda equina

Tumors of the conus when fully developed cause anesthesia of the external genital organs, the perineum, anus, the inferior gluteal region and the posterosuperior area of the thighs. The anesthesia may reach the genito-urinary mucosa. Paralysis of the bladder and rectum with incontinence or retention and "involvement of the sexual function and of the sensation of ejaculation," pain, motor power of the legs unchanged while the reflexes are normal, are the usual symptoms (Gordon).

With tumors of the cauda equina the prominent symptoms, if the growth does not involve the conus, are pain in the lumbosacral region and in the legs. In advanced cases movement aggravates the symptoms.

Paresthesia and anesthesia within the region of the perineum, anus, and genitals, is the rule.

Paralysis is usually present from the beginning of the tumor pressure, is flaccid, is soon associated with *atrophy of the muscles* and the *reaction of degeneration.*

Sphincter symptoms are usual, either early or develop as the disease progresses, and with the advancing infiltration, bed sores, cystitis and sepsis are not uncommon.

The prognosis when the above symptoms are included in the clinical history is unfavorable. Sphincter paralysis, bladder and septic symptoms are permanent; no treatment will relieve them.

After a period of varying length with symptoms of *compression*

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myelitis and sepsis, death follows. The more frequent growths are sarcoma or fibrosarcoma. The size of the vertebral canal permits of considerable growth before pressure symptoms follow.

Tumors may involve the conus and cauda equina at the same time.

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7. *Caisson Disease*

See Diseases Due to Physical Agents (Section XII).

8. *Affections of the Blood Vessels of the Spinal Cord*

(a) Anemia of the Spinal Cord

Anemia of the cord may follow *arterial obstruction; local anemia may lead to necrosis and consecutive inflammation.*

Spinal anemia is a secondary process, a part of a *general anemic condition* which leads to symptoms which have been characterized by some as "*spinal irritation.*" There are forms of spinal anemia which are in fact *mild types of myelitis* and are known as "*funicular myelitis.*"

The syndrome of persisting symptoms associated with *pernicious*

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anemia which were originally fully described by Lichtheim, and to which I have given the name of *"Lichtheim symptoms"* are fully considered in the chapter on *pernicious anemia.*

The prognosis of all forms of anemia of the spinal cord necessarily depends upon the underlying cause.

Symptoms of anemia accompanying the *grave constitutional disturbances* persist, and *yield* only to the successful treatment of the primary disease when that is possible.

Embolic and thrombotic obstruction of the abdominal aorta and its compression cause paraplegia; these are rare, and offer an unfavorable forecast.

Complete anemia of the spinal cord from whatever source at once leads to loss of function and death, if not promptly relieved.

Anemic conditions of the spinal cord materially influence symptoms and prognosis in the terminal stages of leukemia, in cases of ulcerative endocarditis, malignant malaria, carcinoma with metastases, some cases of tuberculosis, suprarenal disease and the chronic intoxications, including lead poisoning and alcoholism. With many of these there are *changes of an organic nature in the lateral and posterior columns of the cord.*

Symptoms *referable to the spine* dependent upon simple anemia, chlorosis, anemia due to sudden depletion (hemorrhage, accident, etc.) all offer an encouraging prognosis.

(b) Hyperemia of the Spinal Cord

Active hyperemia of the cord, independent of other disease, is so rare as to require no consideration; it is a question whether it ever occurs save as the distended vessels mark the initial stage of myelitis or meningomyelitis.

Passive spinal congestion is also exceedingly rare; I have no data, either clinical or pathological, which justify its separate consideration.

Hematorrhachis and *hematomyelia* are separately considered.

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(c) Spinal Endarteritis—Arteriosclerosis
(d) Spinal Embolism and Thrombosis

Changes in the arteries which supply the cord are more frequent than is generally supposed, and, disregarding specific arteritis which is separately considered, lead to either transitory or permanent symptoms in accordance with the extent of the underlying lesions and their location.

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Change in the spinal blood vessels, particularly endarteritis, is an important factor in many forms of spinal disease. Gradually increasing symptoms in patients beyond forty-five or fifty years of age, with or without evidences of general arteriosclerosis in which there are no positive etiologic factors, are in the majority of cases due to sclerosis of the vessels which on post mortem examination prove to be peri- or endarteritic, often resting on a specific basis, with or without involvement of the meninges (gummata), to the obliterating type of endarteritis, or changes in the larger arteries (vertebral, anterior or posterior spinal), often including miliary aneurisms.

The prognosis is only favorable in syphilitic cases in which the true character of the disease has been appreciated early and the patient rationally treated. The prognosis of *arteriosclerosis of the spinal vessels,* large or small, is not encouraging. In many cases the process remains latent during long periods, in others the advance is surprisingly rapid, while in a third class there may be advanced thickening of the spinal vessels without subjective or objective symptoms. In patients who have general arteriosclerosis including cerebral invasion with spinal endarteritis, there may be a long period of helplessness, mental weakness, urinary incontinence with other uncontrollable symptoms and death follows either after coma, due to a septic condition resulting from the cystitis, which finally develops in such cases, intercurrent infections (pneumonia, etc.), or cerebral miliary aneurism may lead to apoplexy.

Advanced change in the spinal vessels, non-specific, cannot be overcome by medical treatment. Emboli may occasionally block the spinal arteries leading to immediate symptoms, the latter depending upon the artery involved. The vertebral artery may be the seat of embolic block which is promptly washed onward without lasting symptoms. Cerebellar symptoms in such cases are prominent. In one of my cases there was repeated blocking of the vertebral artery, with chronic cardiopathy and arteriosclerosis, in which the patient finally developed cerebral symptoms without recurrence of embolism. The prognosis of a large number of the acute and chronic diseases of the cord is often influenced by *thrombosis* of one or more of the medium sized or smaller arteries of the spinal cord with advanced endarteritis.

Sudden paraplegia is not infrequent in the subjects of *organic heart disease* in which *embolism of the cord* is the cause of the symptoms. In most of these cases there are at the same time infarcts with other organs —spleen, kidney or the brain. In these cases the prognosis is unfavorable. With malignant septic endocarditis there are occasionally symptoms of spinal embolism with other infarcts; the prognosis is uniformly bad.

Senile paraplegia offers an unfavorable prognosis. The paralysis as the disease advances, becomes more and more spastic, and if the patient lives long enough, contractures with exaggerated reflexes may develop.

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In these cases there are often associated degenerative changes in the brain (senile dementia, etc.). The prognosis is absolutely bad.

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V. Diseases of the Spinal Membranes

1. Hemorrhage into the Spinal Membranes and Cord

(*Spinal Hemorrhage, Hematomyelia* (*Hemorrhage into the Cord*), *Hematorrhachis* (*Hemorrhage into the Membranes of the Cord*), *Meningeal Apoplexy, Pachymeningitis spinalis hemorrhagica interna*)

Causes.—The cord is so well protected from injury that hemorrhage into its substance or membranes due to traumatism, except from crushing accidents, stab or gunshot wounds, is seldom. Ordinary accidents are not to be considered as a frequent cause of spinal hemorrhage.

Hemorrhage due to disease is also rare.

Occasionally *arteriosclerosis* and *fatty degeneration* cause limited hemorrhage.

Spontaneous hematomyelia occasionally arises in young subjects without known cause or with *purpura.* One such case of *suddenly arising paraplegia* with other positive evidences of purpura I saw in a girl aged fifteen years who made a perfect recovery.

Symptoms following Hemorrhage.—*Hematomyelia may lead to the formation of cysts* with persisting paralysis and focal symptoms. Such cases are favorable if recognized early and are promptly operated.

Syringomyelic symptoms may develop after hemorrhage into the membranes and cord.

All of our cases developed suddenly without loss of consciousness, but there was almost always complete paralysis. The extent of the paralysis, shock and subsequent course depend upon the location and extent (amount of destruction) of the hemorrhage.

Sphincter symptoms may develop after a few days and in those cases which live or are subacute, there are *bed sores* and symptoms of *transverse myelitis.*

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The prognosis of traumatic cases is as a rule bad as the injuries are severe, extensive and destructive; they usually show external evidences of the accident.

The development of some paralysis and symptoms of pressure is immediate; the increase is rapid, depending on the amount of blood and the compression. *The higher the hemorrhage the worse the prognosis.*

Injuries with *hemorrhage into the cervical cord* often involve the *medulla* and *pons*, when they cause prompt death.

Purpuric cases when not malignant, if not extensive or unfavorably located as in the case above mentioned, offer a good prognosis.

The cases in which malignant disease, disease of the vertebrae, caries and suppurative processes lead to hemorrhage, usually die with the symptoms of compression myelitis.

There are *small meningeal hemorrhages* associated with the *acute infections* which are not of great prognostic significance.

Aortic aneurism has occasionally ruptured into the vertebral canal and caused sudden death.

2. *Spinal Hematoma*

Pachymeningitis hemorrhagica interna

Occasionally there are evidences of spinal pachymeningitis hemorrhagica interna in which there are coincident *hematomata* in the brain and spinal cord. These are found in paretic subjects and other forms of insanity, with the grave and the pernicious forms of anemia and in cachectic children. The condition is rarely diagnosticated *intra vitam.*

When associated with brain hematoma, the spinal fluid is clear or yellowish in color; there is slight leukocytosis or lymphocytosis, some blood coloring matter; pressure is usually increased; albumin is also increased; globulin is present; and with infectious cases the staining and cultural methods assist in diagnosis and prognosis.

The patients die of intercurrent diseases—not often from the hematoma directly.

3. *Spinal Meningitis*

There are but few cases of spinal meningitis of primary origin. The most frequent forms of meningitis are *cerebrospinal fever or meningococcus meningitis, tuberculous meningitis,* and *chronic syphilitic spinal meningitis.* These are all separately considered (See Cerebrospinal Meningitis, Chapter on Tuberculosis and Syphilis of the Nervous System). *Pneumococcus meningitis* (usually cerebral) is also separately considered (See Pneumococcemia).

Cases of *meningismus* are associated with the acute infections and are of cerebral origin, rarely spinal.

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Strümpell reports cases of cerebrospinal meningitis following empyema and pulmonary gangrene; these cases are always grave.

(a) Spinal Pachymeningitis

Spinal pachymeningitis or inflammation of the dura mater may be either internal or external. When it begins in the dura and spreads from that membrane, it is *internal*, when the dura is involved from conditions outside, it is *external*.

External Spinal Pachymeningitis.—External spinal pachymeningitis is therefore almost always secondary to diseases of the spinal vertebrae, caries, tuberculosis, carcinoma, bed sores, suppurative processes, thrombosis, retropharyngeal abscess, syphilis and erysipelas.

External pachymeningitis may follow *surgical operations* near the spine with *consecutive infection*.

The prognosis of external pachymeningitis is always grave because the cause is not often amenable to treatment, and the invasion of the membranes adds enormously to the danger.

The lumbar fluid with pachymeningitis externa, due to caries and cancer, shows albumin increase without marked increase of lymphocytes. The fluid is yellowish and coagulates spontaneously.

Internal Spinal Pachymeningitis.—Internal spinal pachymeningitis is exceedingly rare. Inflammation does not limit itself to the dura; there is usually a predominating leptomeningitis. The prognosis is always grave but in occasional cases the patient is brought safely into port after weeks of close attention and care, with but little damage.

(b) Hypertrophic Cervical Pachymeningitis

Charcot in 1871 first described hypertrophic cervical pachymeningitis which is a *chronic inflammation of the cervical dura mater associated with enormous fibrous thickening of the membrane.*

The *periosteum* is also involved in most cases; the dura is adherent to it and cannot be easily separated. *The symptoms of compression are in the ascendency.*

Degenerative processes follow in the motor nerves and muscles of the upper extremities, with secondary degeneration of the pyramidal tract in the cord.

The symptoms of involvement of the motor fibers are in evidence and from the beginning progressive; the pain is at first severe (periode douloureuse of Charcot) and continues several months, after which there is an advance to *motor paralysis and muscular atrophy.*

Spastic paralysis of the lower extremities develops as the case becomes more and more chronic without marked atrophy of the leg muscles and

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without change in electric excitability, while the arms show decided atrophy and the reaction of degeneration.

In the late stage, bladder symptoms are not infrequent. One of my cases, a man, recovered completely after two years with but little damage, some contractures, but not sufficient to prevent return to his grocery.

As a rule the disease is chronic and the paralysis persists unchanged during many years. The disease may become stationary in any one of its stages. The prognosis is always grave, and acute complications or progression may lead to death.

There is a class of cases usually syphilitic, in which there is great sensitiveness along the cervical spine, persisting pain in the neck and along the arms, without paralysis but with motor weakness, with paresthesia and hyperesthesia, at times anesthesia of the hands. These cases are probably due to cervical periostitis with more or less pachymeningitis; they tend to recur, are favorably influenced by specific treatment and counter irritation.

(c) Acute Spinal Leptomeningitis

Acute inflammation of the arachnoid rarely limits itself to the spine but involves the cerebral membranes as well. (The epidemic form of cerebrospinal meningitis (meningococcus meningitis) is separately considered.)

In occasional cases the spinal symptoms in acute non-epidemic leptomeningitis predominate. The disease in my experience is so rarely idiopathic as to require no further mention than it has received in its consideration as a complication of many infections to which the reader is referred (particularly the Chapters on Tuberculosis, Syphilis, Erysipelas, Pneumonia, Typhoid Fever, Septicemia, Scarlet Fever; also Diseases of the Nasal Fossae and Skull and Chronic Nephritis, Arteriosclerosis and Gout).

Whenever the diagnostician finds the symptoms of acute leptomeningitis, his first duty is to establish the primary cause—which is easily accomplished in almost all cases—after which prognosis is comparatively easy. Lumbar puncture and blood-cultural methods are of enormous assistance.

In all cases which originate in the spine, extension to the cerebral meninges is to be expected.

(d) Chronic Spinal Leptomeningitis

Chronic spinal leptomeningitis as a primary disease is infrequent. I agree with Strümpell that in the cases so diagnosticated originally, in the end some other condition is found.

Syphilis of the spine with chronic meningeal changes is separately considered.

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Whenever the diagnosis of chronic spinal leptomeningitis is justified, the disease is secondary and the primary cause must be unfolded before prognosis is possible. It is a part of tabes dorsalis, myelitis, multiple sclerosis and progressive muscular atrophy. In most of these there are adhesions to the dura.

Syphilis and tuberculosis, metastases and multiple sclerosis will be found to be among the most frequent causes.

(e) Postbasic Meningitis

(*Sporadic Spinal Fever*)

I also mention this form of cerebrospinal meningitis in connection with the epidemic form of the disease. Lees and Barlow call attention to these cases in which there are tonic spasms which are limited. In over one-half of these cases (50 post mortems were made) of postbasic meningitis, the spinal membranes were involved. These cases are considered sporadic and always serious. The mortality is high; rarely in my experience below 50 per cent. Strümpell believes that the so-called idiopathic cases are identical in their etiology with the epidemic form. I believe that all cases of postbasic meningitis should be considered infectious cerebrospinal meningitis.

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C. Diseases of the Brain and its Membranes

I. Diseases of the Membranes of the Brain

1. Pachymeningitis—Inflammation of the dura mater

(a) Pachymeningitis interna
(b) Pachymeningitis externa.

(a) Pachymeningitis interna

(*Pachymeningitis hemorrhagica interna*)

General Considerations.—Unquestionably there are many cases of hemorrhage of the dura mater resulting from traumatism which give rise to but few or no symptoms, often recover without leaving permanent damage, or are accidentally discovered post mortem.

The majority of cases of internal pachymeningitis due to traumatism

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are associated with fractures of the cranial vault or its base. These cases are almost always associated with profound cerebral disturbances, are serious and are likely to lead to death after a train of meningeal symptoms, including loss of consciousness, the Kernig symptom, and changes in the spinal fluid as shown by lumbar puncture. The fluid may escape (Plaut, Rehm and Schottmüller) under normal or increased pressure. The cases in which the fluid is markedly hemorrhagic with high pressure offer an unfavorable outlook. The fluid in occasional cases of pachymeningitis may continue clear or yellowish when blood coloring matter has been present during varying periods. The appearance of the fluid depends very largely on the primary cause of the internal pachymeningitis and the chronicity of the individual case. The fluid may show no red blood corpuscles, in spite of the presence of blood coloring matter and a yellow tinge. This is also true of chronic cases. *Albumin* is present with a positive *globulin* reaction.

Failure to demonstrate microscopically or culturally the presence of microörganisms with positive infection, has no bearing on the prognosis of the individual case (Schottmüller). In non-traumatic cases the *cellular count* may continue normal or slightly increased without influencing the forecast.

In occasional cases, cysts with multiple partitions filled with serum may follow hemorrhage and lead to focal symptoms (hygroma durae matris). These cases, when recognized and localized early, treated surgically offer some encouragement for restoration of function when this is disturbed. The prognosis of these cases is good in proportion to the time of operation (early is best), the resistance of the patient, the exact localization of the cyst, and the escape from injury of the surrounding brain tissue.

Causes and Development.—*Chronic alcoholism* is often the cause of pachymeningitis. Many of these cases are finally complicated with ependymitis and bronchopneumonia—these are almost uniformly fatal.

Paresis with acute hemorrhagic pachymeningitis interna leads to death with pressure symptoms in from three to four days. In the chronic cases the course is prolonged—may cover months—and death often follows acute exacerbations.

Senile dementia is not infrequently associated with dural hemorrhage in its terminal stage. *Purpuric conditions*, non-malignant, may develop internal hemorrhage (pachymeningitis) and yet, if this is not too extensive, recovery may follow. If the hemorrhage is extensive and there are complications, if the infection is malignant, then the prognosis is bad. Cases dependent on *nephritis and chronic cardiopathies* are always serious. *In all of these cases the amount of cerebral compression becomes an element of the greatest importance in prognosis.*

Persistent and unchanging symptoms of compression or increasing

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evidences of pressure are among the unfavorable features of all cases of pachymeningitis.

Streptococcus, pneumococcus and syphilitic infections when the cause of pachymeningitis always justify a guarded prognosis. Of these, the syphilitic cases are the most favorable. *Erysipelatous infection with acute pachymeningitis,* particularly in *alcoholics,* is among the gravest of all forms of the disease. While recovery is rare, it is not impossible. The clinician is not to be deceived by periods of remission of symptoms in chronic cases; such improvement (usually of the sensorium) is only transitory, and deep coma is likely to follow at any time. Some acute cases remain unconscious during several weeks (usually syphilitic) and gradually mend and recover. In these cases the pulse may be persistently small and feeble, breathing irregular, temperature not elevated. The complicating paralyses depend upon the location of the hemorrhage. The cranial nerves are rarely involved.

Convulsions of the jacksonian type are occasionally present; when dependent upon cyst formation or when uncomplicated, surgical interference may save the life of the patient.

Coma long continued is always unfavorable. Pernicious anemia in its terminal stage may cause dural hemorrhage. This is also true of the *leukemias, hemophilia,* and *malignant endocarditis.*

Puerperal sepsis and scarlet fever with pachymeningitis are almost always fatal.

The chronic form of internal pachymeningitis may cover a period of years, with acute exacerbations and repeated remissions. Unquestionably a small proportion of these cases in which the process is limited, may recover, but in no case should the prognosis be given unguardedly. This conclusion is justified by the post mortem evidence of chronic pachymeningitis in subjects who presented no symptoms of the lesion during life.

The prognosis of hemorrhagic pachymeningitis dependent upon meningeal hemorrhage has in a number of reported cases been favorably influenced by lumbar puncture and surgical intervention (Michaux, Jaboulay, Neisser-Cushing, Seitz, Curschmann and Devreigne).

(b) Pachymeningitis externa

General Considerations.—Pachymeningitis externa is, according to Ernst, a *periostitis* involving the skull and external surface of the dura which is in close contact with the bone. The process is likely to be limited—localized—and may lead to pus accumulation (abscess), i. e., extradural abscess, or may lead to localized *osteomyelitis* of the skull.

Most external pachymeningitides are secondary and follow middle ear inflammation, mastoid disease, tonsillar infection, or fractures of the skull.

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Development.—The disease may complicate influenza, scarlet fever, measles, diphtheria, typhoid fever and smallpox. Ernst has found among the leading microörganisms, strepto-, staphylo-, diplo-, and pneumococci, and the pyocyaneus.

I have seen a number of cases in which *destructive specific disease of the skull* has led to pachymeningitis externa with fatal result.

Cases of *erysipelas* with this disease have shown a very high mortality.

While the majority of cases are secondary and offer an unfavorable prognosis, when the disease is not extensive and is promptly treated surgically there are some cases which recover. Gowers has called attention to cases which are *primary*, which are acute in their course, leading to prompt suppuration between the dura and the bone. These cases, however, are more likely to be spinal—rarely cerebral.

The prognosis of external pachymeningitis depends on the malignancy and location of the primary infection, the extent and location of the injury in traumatic cases, as well as the extent of the meningeal complication, the amount of compression and location of the brain lesion, if any, in all cases. External pachymeningitis offers the best prognosis of all the meningitides. There will always be a large number of cases of external pachymeningitis which will remain unrecognized during life because of the proximity of the primary disease, the symptoms of which remain in the ascendency, obscuring those of the complication.

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2. Leptomeningitis

(*Inflammation of the pia mater and arachnoid*)

(a) Purulent leptomeningitis
(b) Serous leptomeningitis
(c) Chronic leptomeningitis.

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(a) Purulent Leptomeningitis

Causes.—Pus-producing organisms from the surrounding tissues or from neighboring organs infecting the cerebral membranes are the cause of this type of *meningitis.*

Metastatic leptomeningitis is less frequent than direct infection from the nose, middle or internal ear, the mastoid, caries of the temporal bone, direct injury of the skull with associated infection, abscess of the brain and meningitis by contiguity (per continuitatem) (Jacobsohn), or the disease may follow nasal operations (removal of polypi or bone tissue with subsequent purulent infection), influenza, and not infrequently latent pus deposits in the brain or the surrounding tissues.

It is not unusual to find that middle ear suppurations, supposed to have been fully controlled, i. e., healed, lead to the development of meningeal symptoms without a long prodromal period, and meningitis may promptly follow.

The *microörganisms* most frequently responsible for purulent leptomeningitis are the pneumococcus, meningococcus (cerebrospinal meningitis separately considered), streptococcus, typhoid bacillus, staphylococcus, and the bacillus coli communis.

Metastatic leptomeningitides are usually dependent upon pneumonia, ulcerative endocarditis, typhoid fever, polyarthritis (rheumatism), scarlet fever, measles or smallpox. Other acute infections may be complicated by this serious condition.

Meningitis occurring with the acute infections may not always be due to the same cause as the primary disease but mixed infections are to be considered in offering a forecast (See Pneumonia).

Its Occurrence as a Complication.—Quoting from Edwin Bramwell: "The relative frequency of leptomeningitis as a complication and cause of death is considered."

"Osler found meningitis in 8 of 100 autopsies, while among 253 cases of pneumonia examined after death, Aufrecht met with 7 in which meningitis was present. Musser and Norris found a post mortem record of meningitis in 180 of 4,833 cases of pneumonia. . . . Anders in his analysis of 1,674 cases of erysipelas does not refer further to it than to remark that it is an occasional complication."

"Typhoid fever is very rarely complicated by true meningitis. Cole has collected 21 cases of meningism, serous and purulent meningitis, from the literature, and 6 instances were present in the Johns Hopkins Hospital series of 1,500 cases of typhoid fever analyzed by McCrae."

"Dubois, in 1903, collected 11 cases in which purulent meningitis was due to Pfeiffer's bacillus."

In the German army of 55,263 cases of influenza there were but 4 cases of meningitis.

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It may be assumed for diagnosis and prognosis that *when meningitis of the convexity is bilateral* it is due to pyogenic organisms; when *unilateral* it is likely to be secondary to middle ear disease.

Basilar meningitis is usually but not always of tuberculous origin; traumatism, nasal disease (nasal operations), may open the avenue for infection which may spread to and from the base to the meninges.

Postbasic purulent meningitis is likely to be of epidemic meningococcus origin.

Councilman reports 60 consecutive leptomeningitides in which he found the pneumococcus in 18 cases, streptococcus in 18, meningococcus in 21 and staphylococcus in 2.

The pneumococcus and meningococcus are responsible for the majority of the primary meningitides (Marchal), (50.5 per cent are due to the meningococcus, 42 per cent to the pneumococcus).

I have frequently referred to leptomeningitis as a complication of the acute infections in other chapters.

Meningitis following erysipelas is of the suppurative type, and offers an unfavorable prognosis.

Leptomeningitis with metastatic parotitis in my experience has been almost uniformly fatal. Oppenheim has had a more favorable experience with his cases. It is held by Dopter, who has considered this subject, that most of these cases are due to the serous type of the disease.

Infectious sinus thrombosis with meningitis is promptly associated with fully developed symptoms, and death usually results.

General Conclusions.—*No case of leptomeningitis, however mild the symptoms may appear during the early stage of the disease, should be considered otherwise than serious.*

Cases in which the process is limited and within a safe area for operation offer a much better prognosis than do the other forms of the disease in which the process is diffuse.

Cases of otitis with symptoms of meningismus which are treated radically and early, often lead to recovery without the full development of meningitis.

Cases in which the Kernig symptom is present with *involvement of the sensorium,* with moderate coma, gradually increasing or deep coma, rarely recover.

Muttering or wild delirium with the Kernig symptom, with or without paralysis of one or more of the cranial nerves, usually leads to stupor which in the course of twenty-four to forty-eight hours is followed by deep coma and death.

In most cases active delirium is followed by stupor and coma.

Active delirium (delirium ferox) with great unrest early, the Kernig symptom and increasing elevation of temperature is always ominous—

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usually fatal. Early and persistent vomiting robs the patient of resistance and adds an element of danger.

The addition of paralysis of the cranial nerves, one or more, proves the presence of basilar meningitis.

Optic neuritis is not to be interpreted favorably.

Inequality of pupils with other symptoms of paralysis (faulty reaction), and acute symptoms are unfavorable.

Early convulsions in children are less significant than in adults, but in both, in all stages of the disease, they are of serious import.

Involuntary discharge of urine and feces is always unfavorable—showing deep involvement of the sensorium.

An abnormally slow pulse early, soon (in two or three days) *followed by a rapid, small and erratic pulse,* argues in favor of a rapidly increasing and fatal process.

Primary pneumococcus meningitis may be considered as *almost uniformly fatal. The exceptions are so rare* that the diagnosis may be questioned when a patient recovers.

Paralysis of the extremities, one or more, is as a rule evidence of an advanced process.

The loss of the tendon reflexes after their persistence during several days should be unfavorably interpreted.

Occasionally *otitic meningitis* recovers after rupture into the middle ear. In such cases we must always consider the greater likelihood of cerebral abscess and not a simple uncomplicated purulent leptomeningitis.

Gowers has reported two cases of recovery from *puerperal meningitis.*

Mulhit and Tanon have seen recovery from *gonococcus meningitis.*

The prognosis of *parotid meningitis* is comparatively favorable (Oppenheim).

Purulent meningitis following orbital disease or the surgical treatment of the orbit or eye have in my experience finally been diffuse and uniformly fatal.

The warning of Hippocrates, that no injury to the head is to be lightly regarded in spite of the absence of immediate symptoms proves that he appreciated the possibility of infection of the meninges long after traumatism.

It is possible for purulent meningitis to develop after injuries to the head in which there is no break of the skin or evident external infection, when pathogenic organisms are already present in the blood (Huisman, H. Curschmann [Raecke].

Cheyne-Stokes breathing is always ominous and usually fatal; it is indicative of reduced excitability of the respiratory center.

Rigidity of the neck, painful movement of the head with retraction—*opisthotonos*—shows involvement of the meninges of the cervical cord.

The *Kernig symptom* to which we have already referred was present

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in over 94 per cent of our cases and should always be interpreted in the presence of other symptoms of meningeal irritation as indicative of meningitis. An occasional error may be made by such reasoning but this will be exceedingly rare in the practice of the cautious clinician, and the acceptance of the rule will often lead to early diagnosis and prognosis.

Lumbar Puncture.—The knowledge gained from lumbar puncture in acute leptomeningitis is most valuable for diagnosis and it is of considerable prognostic value as well. Repeated lumbar puncture has also, in a fair number of cases, led to improvement of symptoms, and if the conclusions of Kummell, Curschmann, Voss, Bokay and others are confirmed by added experience, we will save at least a small proportion of cases by the timely and repeated withdrawal of lumbar fluid, which without such treatment, present a more serious forecast.

The prognosis depends in a measure upon the virulence of the infecting agent. Purulent meningitis offers a more favorable outlook than does the tuberculous form of the disease. Lewandowski says he never saw recovery when the lumbar fluid gave evidence of streptococcus infection, while he has seen, as all have, recoveries from staphylococcus, and influenza infection. In all of these cases lumbar puncture gives valuable prognostic data. In some cases of fully developed meningitis, there may be no bacterial contamination; with a cloudy fluid, evidence of a limited and localized process, the condition is more favorable than when there is dissemination and positive bacterial contamination of the spinal fluid.

Evidences in the spinal fluid of the proliferation of the infecting agent in the free meningeal exudate is always unfavorable.

Plaut (etc.) insists that the presence of bacteria in the spinal fluid with meningitis is proof of a widespread meningitis—the disease is then no longer limited.

Once the pneumococcus is found in the spinal fluid (the microorganism which is most frequently responsible for the complication), the prognosis is exceedingly grave. When the fluid escapes under high pressure (250-400 mm. of Hg.) and the quantity of fluid is materially increased, is cloudy, not purulent as a rule, the prognosis is unfavorable in the overwhelming number of cases, for the disease may under such conditions be assumed to be advanced.

Polymorphonuclear increase is characteristic of pneumococcus meningitis.

The presence of the *streptococcus viridans* in the lumbar fluid, may prove the association of chronic infectious malignant endocarditis with meningitis often with infarct, and is grave.

In cases which recover there are often remnants of lesions which are destructive and which may lead to deafness of one or both ears, ocular defects, chronic suppurations, hydrocephalus and other serious disturb-

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ances, including mental enfeeblement, paralysis—either limited or extensive.

The *duration* of acute purulent leptomeningitis is variable. So-called "lightning cases" may lead to prompt death—from 24 to 48 hours—with deep involvement of the sensorium early; such histories are not infrequent.

Operable cases may present grave and threatening symptoms during the first day or two; some of these, when localized and drained make satisfactory recoveries.

The *average duration* of the disease is between 12 and 14 days. *Sinus thrombosis or abscess*, without marked—at times no—symptoms, often lead to the sudden development of positive symptoms of leptomeningitis and death in a few days, unless localized.

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(b) Serous Leptomeningitis

(I) Serous Meningitis
(II) Acquired Hydrocephalus
(III) Congenital Hydrocephalus.

Idiopathic Internal Hydrocephalus, Angio-neurotic Hydrocephalus (Quincke)

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(I) *Serous Meningitis*

Serous meningitis (Quincke) often offers a favorable prognosis, and is in all probability dependent upon the same vasomotor disturbances which cause other forms of Quincke's disease or angioneurotic edema. This form of meningitis may be of primary origin.

Serous meningitis may be a complication of the acute infections, pneumonia, typhoid fever, tuberculosis, whooping-cough and measles, in which there is, according to Rothman, lowered virulence of the infecting microorganisms. These cases should be separated from the Quincke type of the disease.

Lumbar puncture gives data in cases of idiopathic serous meningitis which strengthens the diagnosis; the prognosis is more favorable than in other forms of leptomeningitis. The fluid escapes under enormously high pressure, is markedly increased, contains but a trace of or no albumin, but few lymphocytes, and may show the presence of a few bacteria. Marked improvement of symptoms in these cases after puncture is favorable in spite of the fact that exacerbations may follow.

Cases in which the diagnosis of serous meningitis seems justified not infrequently run a self-limited course and heal spontaneously, or if lumbar puncture proves insufficient to drain, puncture of the ventricles has in some cases led to recovery.

Cases in which the pressure is sufficient to force brain substance into the foramen magnum as the result of overpowering edema lead to prompt death, unless lumbar or ventricular puncture or decompression relieve.

(II) *Acquired Hydrocephalus*

Acquired hydrocephalus and idiopathic internal hydrocephalus may run anomalous courses: acute exacerbations may follow a long period of ill-defined or even positive symptoms.

In cases of acquired hydrocephalus death may occasionally follow suddenly after several years of symptoms. There are cases of acquired hydrocephalus with but few symptoms—headaches, vertigo; the neurasthenic state (Oppenheim) in which the disease itself is little influenced by treatment, does not destroy life directly; the patients often die of intercurrent disease after years of indefinite symptoms and chronic invalidism.

Chronic acquired hydrocephalus may heal spontaneously or become latent.

Cases of *acquired hydrocephalus simulating brain tumor* offer an unfavorable prognosis though different patients live during periods of varying lengths.

Acute exacerbations are characteristic of hydrocephalus and may lead to death in a few hours in coma with or without preceding optic neuritis,

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or the end may follow a few days of increasing symptoms of meningitis with final coma.

(III) *Congenital Hydrocephalus*
(*Hydrocephalus internus*)

General Statements.—The appearance of the hydrocephalic child is characteristic, with its enormous head, strikingly prominent forehead, open fontanelles, and small face—expressionless. The size of the face is out of all proportion to the size and weight of the entire head. There is moderate exophthalmos. The fluid increase in the dilated ventricles is often associated with an enormous accumulation between the brain and the dura. The greater accumulation is found in the ventricles as a rule (internus). At term, the child with *congenital hydrocephalus* is often threatened with destruction because the head cannot be forced through the pelvis.

There are data which prove that congenital hydrocephalus may be of the *"family type"*—when several children of the same family are born with the anomaly—or the hydrocephalus may prove to be hereditary. Father and son without syphilitic taint have both been hydrocephalic in my experience.

Occasionally the process is arrested and if originally limited, not far advanced, an approach to normal conditions may follow. Such patients, if there are no other congenital defects may live to the twentieth or twenty-fifth year in comfort, even longer. I have seen children with large heads (hydrocephalus) without improvement in the physical or mental status live during periods varying from four months to eighteen years. There are but few with unchanged hydrocephalus who live beyond the fifth year.

The large proportion of hydrocephalic children die shortly after confinement, or within a few months of birth.

Syphilitic children with small hydrocephalus may improve under treatment, and in occasional cases are cured.

Spontaneous rupture of the hydrocephalus through the membranes into the sutures is exceedingly rare. Huguenin reports nine (9) such cases with five (5) recoveries. Some rupture into the nasal fossa. None of my cases have been permanently benefited by any surgical treatment, lumbar or ventral puncture.

The prognosis of congenital hydrocephalus is not materially influenced by its cause; in the majority of cases the true pathogenesis is doubtful and remains so.

Causes and Development.—*Traumatism* has been assigned, *cachexia, drunkenness, constitutional diseases, syphilis* particularly, have also been considered among the causes of hydrocephalus. In all, the prognosis con-

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tinues exceedingly grave unless as occasionally happens, the process proves to be limited or the fluid is absorbed.

Hydrocephalus in syphilitics may occasionally reach its greatest development at puberty. The slight congenital anomaly may previously have escaped detection.

The development of the brain is almost always materially and unfavorably influenced by hydrocephalus. *Intelligence is blunted and remains so* in the fully developed cases.

Hydrocephalic children are, as a rule, unfit to be received in either public or private schools. About one-eighth of all hydrocephalic children attempt to keep up with their school work: failure is the rule with most hydrocephalic children.

Accompanying *motor paralyses—hemiplegia* or *monoplegia*—are likely to remain; secondary contractures always follow if the children live. Moderate, *unchanging hydrocephalus* may be present without materially influencing the mind; in rare cases, hydrocephalics have been unusually brilliant, talented far above the average man. *Cuvier and Helmholtz* were the subjects of moderate hydrocephalus (Oppenheim and Hauseman).

Hydrocephalic girls present menstrual anomalies—development is comparatively tardy and incomplete.

Complications.—*Epilepsy with hydrocephalus* may be an early complication; it does not yield to treatment. Active treatment, persistent medication, may at times postpone the seizure but does no more.

Spastic paralysis occasionally develops in cases in which there is compression of the pyramidal tract.

Blindness is among the most frequent complications involving the special senses, and is never relieved by treatment. Other ocular anomalies, including *strabismus,* as well as *nystagmus, choroiditis, optic atrophy,* once established remain uninfluenced by treatment. Involvement of other cranial nerves is infrequent.

The *spinal fluid* offers nothing which, after the diagnosis has been made, favorably influences prognosis.

There is as a rule, increased pressure; the fluid is normal in appearance also the cellular elements. Acute inflammatory (cerebral or cerebrospinal) complications are promptly recognizable by change in the spinal fluid in accordance with the nature of the disease.

Intercurrent disease is a cause of death in cases which live beyond the first few months; these include gastro-intestinal, pulmonary, and occasionally other infections.

Among my cases of hydrocephalus only one lived to be 30 years of age. Gall reports one case which died in his 54th year.

Tuszek and Cramer had a hydrocephalic patient with idiocy who died in his thirty-second year of infection (phlegmon). There are many with

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congenital hydrocephalus who live with almost no human attributes during periods of varying length.

Syringomyelia only occasionally develops in cases of hydrocephalus; naturally its progress cannot be halted.

There is occasional development of *suprarenal disease* with hydrocephalus (Czerny).

Children with marked hydrocephalus rarely learn to walk and are unable to stand or sit without support because of the enormous weight of the head.

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(c) Chronic Leptomeningitis

Chronic changes in the membranes of the brain (pia-arachnoid) are not unusual complications of alcoholism, chronic toxemias, chronic nephritis, diabetes mellitus, encephalitis, dementia paralytica, or jacksonian epilepsy, and may follow traumatism.

Chronic adhesive leptomeningitis when circumscribed with adhesions may simulate brain tumors.

In all of these conditions the prognosis depends upon the ability to influence or remove the underlying cause. As a rule this is impossible, though occasionally surgical interference proves curative, or latency follows.

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3. Syphilitic Cerebral Meningitis

See Syphilis.

4. Tuberculous meningitis

See Tuberculosis of the Nervous System—Chapter Tuberculosis.

5. Cerebrospinal Meningitis (Epidemic)

See Infectious Diseases.

II. Circulatory Disturbances of the Brain

1. Anemia

General Considerations.—Anemia of the brain is of secondary origin, and the prognosis therefore depends upon the underlying cause.

The prognosis of *brain anemia per se which follows sudden loss of a large quantity of blood* is not bad. It very often happens that there are symptoms of alarming anemia following the loss of blood during labor (placenta previa, post partum hemorrhage) in which the patient is thoroughly exsanguinated, and with the control of the hemorrhage gradual return to health is the rule.

Associated Symptoms.—The *cerebral anemia secondary to other controllable hemorrhages* offers a favorable prognosis.

The anemia associated with the benign chloroses and anemias is usually favorably influenced by treatment, and leads to prompt improvement and gradual return to health as the general condition of the patient improves. Marked evidences of cerebral anemia with *pernicious anemia, the leukemias, splenic anemia, malignant* or *pernicious malaria, cachexia, cancer, phthisis,* are usually associated with grave constitutional symptoms and often precede death by only a few days, particularly when there is stupor and coma.

Anemia due to vascular spasm, the latter resulting from advanced arterial disease, may yield temporarily; the patient may die of intercurrent disease. The prognosis of the underlying fault is bad and in the majority of cases the disease advances; *vascular spasm* with associated anemia recurs. Hyperemia may finally displace the anemia, or in some cases *cerebral apoplexy* ends the scene.

The prognosis of *cerebral anemia dependent upon insufficient heart strength,* unless the latter is due to transitory or removable causes, is always grave.

Localized cerebral anemia which depends upon obstruction to the free flow of blood through one or more of the cerebral vessels offers an unfa-

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vorable prognosis; if it persists for any length of time, sudden death may follow or the brain tissue may undergo degenerative changes, i. e., *softening* (See Embolism and Thrombosis).

Transitory paralyses are often due to anemia of the brain following *vascular spasm* (See Arteriosclerosis). The cerebral anemia due to senile degeneration remains almost entirely uninfluenced by treatment.

The ordinary and frequent anemia of the brain associated with the phenomena of the *"faint spell"* is without serious import unless dependent on organic cause. Many individuals develop cerebral anemia—faint—on slight cause, are materially inconvenienced by this idiosyncrasy, but the prognosis, so far as life is concerned, is always good.

The delirium of inanition is due to anemia of the brain; its prognosis depends entirely upon the nature of the primary cause.

Cerebral anemia with convulsions is always ominous, and is as a rule, dependent upon grave primary and organic disease.

Cerebral anemia with unconsciousness, dilated and immobile pupils offers an unfavorable forecast.

Lively pupillary reaction with cerebral anemia is always encouraging.

Marked cerebral anemia with uremic intoxication is always unfavorable.

Cerebral anemia with lead poisoning, acute delirium, and other evidences of lead *encephalopathy,* is exceedingly grave and calls for a guarded, usually a serious prognosis.

Oppenheim reports cases of *retrobulbar neuritis* following profuse hemorrhage and anemia of the brain. Ziegler found *parenchymatous degeneration of the optic nerve;* and Scagliosi found marked changes in the ganglionic cells of the brain, and so did Soukhanoff. Bouveret and others have found *localized edemas of the brain* with anemia, and the former reports one case in which after an alarming *hematemesis, hemiplegia and aphasia* developed. Such complications either lead to prompt death, or the improvement following is surprisingly rapid.

Paralyses which are occasionally associated with the secondary anemia of childbirth (due to hemorrhage) are as a rule, due to *arterial or venous thrombosis.* The prognosis depends entirely on the way in which the patient reacts from the hemorrhage and the extent and location of the thrombus, as well as the gravity of the primary disease.

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2. *Hyperemia of the Brain*

(*Congestion of the Brain*)

General Considerations.—*Hyperemia of the brain is symptomatic, and like anemia must be considered to be of secondary origin—never a condition per se.*

We have but scant knowledge of the true pathology of cerebral congestion and should not lightly assume that it is often a chronic condition. The results of post mortem examinations are almost entirely negative: no characteristic lesions have been found which explain the symptoms.

A *large number of unexplained cases are unquestionably due to toxemia of some kind.*

Experimentally no marked increase in the quantity of arterial blood can be produced suddenly; an increased flow of blood through the brain follows abnormally strong systolic contraction and consecutive rise of arterial pressure (Leonard Hill).

Sir William Gowers has said: "Of all regions of cerebral pathology, that of congestion of the brain is most obscure. We have very little precise knowledge regarding it; and as is often the case, theory has flourished in proportion to the deficiency of fact."

"It is highly probable that many symptoms have been erroneously ascribed to cerebral hyperemia which should be placed at the door of cerebral venous congestion, or of anemia of the brain" (Leonard Hill).

Hill further concludes:

"I. Arterial hyperemia of the brain does not exist as a pathological state.

II. Sphygmometer readings of arterial pressure in man show that the tension of the cerebral arteries is constantly varied by change of external temperature, exercise, sleep, bath, food, etc. Such variations are purely physiological.

III. There is every indication that the quality of the blood which flows through the brain is of greater importance than the quantity.

IV. Mental exhaustion probably does not arise during the stage of hyperemia produced by continued over-effort, but supervenes at that period when the circulatory mechanism begins to fail, and venous congestion accompanied by a deficient supply of oxygen is the fate of the exhausted cerebral centers."

Nevertheless, there are clinical conditions which arise which remain unexplained, requiring consideration, and which suggest the presence of a brain which may be abnormal, filled with blood, presenting characteristic symptoms. To these I refer in the following pages.

Classification.—Primary conditions in which there is associated acute cerebral hyperemia are either (a) active, or (b) passive.

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In framing prognosis we must suspect that in both forms of cerebral hyperemia the blood vessels are over-distended; that the failure to empty the capillaries is responsible for the symptoms; that, as Herter has demonstrated, the "brain suffers from a deficiency of oxygen in consequence of the stasis, but in passive congestion there is also an excessive accumulation of carbonic acid in the capillaries."

With *active hyperemia* the arteries are overfilled with blood, with *passive hyperemia* the veins are overfull.

Five-sixths of all cases of acute cerebral hyperemia were formerly supposed to be active. In the light of our present knowledge we assume that the majority of these are toxic or due to vascular fault. There are many causes which may be responsible for both varieties of cerebral hyperemia, and these demonstrate the enormous difficulties encountered in offering a dependable prognosis.

Among the *leading causes* which should be considered are, *hyperpyrexia, infection—acute and chronic—sunstroke, faulty ventilation, overeating, violent exercise, excitement, long continued constipation, pressure* (particularly neck constriction) any *circulatory fault* which obstructs the return cerebral circulation, *alcohol, highly seasoned foods, opium, belladonna, quinin,* the *salicylates, amyl nitrite, nitrites generally, tumors of the neck, erysipelas, localized brain disease, including tumor, hypertrophy of the left ventricle, myocardial insufficiency, long continued worry, mental over-activity, anxiety, arteriosclerosis* of *the cerebral vessels, emotional acts,* and all *diseases associated with faulty metabolism* including *gout and perverted tissue change.*

During the first stage of acute and active cerebral hyperemia, there are as a rule, no threatening symptoms. With the slow pulse and hypertension which are frequently present, the annoying dreams, increasing mental lethargy, restlessness in bed, sluggish mental processes, failure of sleep to give the expected rest, halting speech, in many cases, heavy head, failing memory from week to week, occasional illusions and delusions, irritability, headache, tinnitus aurium, ocular disturbances, numbness or weakness of one-half of the body at times, cerebral congestion of the arterial variety may at least be suspected and the chances are strongly in favor of progression to the second stage in which the symptoms, according to their severity, may be either *apoplectiform, paralytic, convulsive, soporific, maniacal* or *aphasic.*

In the *apoplectiform variety* of cerebral congestion, sudden loss of consciousness with possible paralysis develops and may continue for several hours or days. The face is rarely paralyzed, respiration in the favorable cases, though changed, does not become irregular or Cheyne-Stokes. In favorable cases there is no involvement of the sphincters. The patient in favorable cases, in a limited time (few hours to one or two days) gradually returns to a dazed condition, somewhat damaged; at times to

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a fairly good condition, with more or less mental depression. When the sleep is deep, prolonged, and the breathing irregular, the prognosis is correspondingly bad.

Gradual increase of *soporific hyperemia with apoplectiform symptoms*, i. e., increasing from a stupid condition to coma, is always unfavorable.

It is characteristic of all forms of cerebral hyperemia to recur, and one form may merge into another.

The *aphasic* and *apoplectiform* varieties may be allied, and recovery may follow. With such a combination, increase of stupor and coma usually leads to death with respiratory irregularity and all the evidences of compression. At least one-half of the cases of so-called cerebral hyperemia are apoplectiform.

In the *paralytic form* there are as a rule no prodromal symptoms but there is a sudden paralysis or paresis, usually one-sided, and from such a condition there may be deepening of all symptoms. In these cases with advanced arterial degeneration, hemorrhage may follow and the paralysis becomes permanent; on the other hand, the paresis may promptly disappear with the relief of the congestion.

The *convulsive forms* of cerebral hyperemia are rarely found before the fortieth year. They may develop with or without prodromal symptoms; may recur at short intervals; may be followed by a period of stupor from which the patient may rally, or following the convulsion and stupor coma becomes deep, and death follows. The convulsions do not occur during sleep. In the severe cases the pupils are at first contracted; there is insensibility to light; vomiting may persist, and the pulse from normal frequency in unfavorable cases becomes rapid, irregular and erratic.

The *soporific variety* is usually due to passive hyperemia; the gradual onset of symptoms without paralysis, more or less headache with dilated pupils slowly lead to coma after days of "heavy-headedness" and a final period of somnolence. Such patients may for years, without advance of symptoms, fall asleep at their work or when in society and particularly when trying to read. *In many of these cases careful search reveals a toxic cause for the soporific state* and it is a question whether in these chronic cases the symptoms are not, as a rule, due to renal invasion—rather than secondary congestion—in spite of the fact that albumin is almost constantly absent from the urine.

Hyperemia with mania—symptoms of marked mental derangement, active delirium—may lead to violence. The symptoms may develop suddenly; paralysis may be an accompaniment; death may follow early, or there may be secondary involvement which finally leads to death.

The *aphasic form* develops suddenly; there is marked aphasia and confusion of thought. If there is improvement, the speech returns slowly, while the patient remains mentally heavy during a number of days. These attacks in some cases recur at short intervals until finally there is

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overwhelming engorgement; pressure symptoms precede a period of coma and death. With advanced arterial disease in this form of hyperemia, secondary changes in the brain are prominent, and the patient does not often recover from a condition in which symptoms are more or less continuous during varying periods.

The overfull condition of the veins of the brain is usually an accompaniment of old age. There is greater tendency to stupor than in the so-called active types of congestion; sleep is disturbed and is likely to remain so; dreams and hallucinations are frequent in the intial or prodromal period.

Passive hyperemia is more serious than are the active types.

The prodromal stage of passive hyperemia may be followed by conditions in which apoplectiform, paralytic, convulsive, soporific, maniacal or aphasic conditions prevail; or as with the more acute clinical types, there may be a mixed symptom complex. Difficulties of differentiating the so-called active from passive hyperemia hardly influence prognosis materially.

The depth of cerebral invasion, the general condition of the patient, the character of the primary and underlying lesion with the extent of cardiovascular and renal disease in all cases, offer the leading data upon which prognosis is founded.

Passive hyperemia of the brain due to compression of the veins by tumors, goiter, mediastinal growths, broken compensation, pulmonary emphysema, "fixed thorax," remain uninfluenced by treatment as a rule, save as growths are removed by surgical menas.

The *"apoplectic habit"* when accompanied with polycythemia, certainly predisposes to cerebral engorgement and cerebral apoplexy.

Occasional cases which suggest hyperemia because of persistent *head symptoms* suffer from *chronic constipation.* Many of these cases are chronic, have acute exacerbations, and yield to rational treatment.

It may be safely assumed that the acute or active variety of hyperemia offers a better prognosis than does the passive, that much depends on the ability of the patient to regulate his habits, particularly during the prodromal stage, as to work, diet and all other factors which directly influence his life.

The apoplectiform and soporific forms of the symptom complex are most grave for they are likely, because of pressure, to fall into coma.

I recognize the fact that the clinical types to which I have referred rest upon an uncertain pathology, but I realize that the clinician frequently meets them in practice and the study of their prognosis therefore, deserves consideration; for the present at least, we can offer no more appropriate chapter for their consideration.

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3. *Occlusion of the Cerebral Vessels*

(*Cerebral Softening*)

(a) Cerebral Embolism
(b) Cerebral Thrombosis.

The plugging of a cerebral vessel either by an embolus, a thrombus, or by pressure, is at once followed by change in the tissues originally supplied.

Nutrition is cut off, and function is either destroyed entirely or materially reduced.

Collateral circulation may come to the rescue, but as a rule there are persistent symptoms so long as the occlusion continues, depending naturally on the artery or vein involved and the brain area included within the distribution of the vessel.

(a) Cerebral Embolism

When a plug is lodged in a cerebral vessel brought to the brain from a distance, it is as a rule, detached from one of the valves of the heart or from the free endocardium. This accident is more frequent in chronic valvular disease, than with acute and non-malignant endocarditis.

Mitral stenosis is the most frequent cause of cerebral embolism. Aortic valvular lesions are less frequently the cause of cerebral infarct than are the mitral anomalies.

The prognosis of all infections in which there is thrombosis in the left ventricle of the heart with final cerebral embolism is exceedingly grave—only rarely does recovery follow.

The *embolic infarcts of acute septic or malignant endocarditis* are not infrequent with that variety of serious, and usually fatal, infection.

The prognosis of embolism must naturally depend upon the *amount of secondary softening* of the brain tissue. The size of the area involved is

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variable. The prognosis is worse when several arteries are plugged or when an embolus leads to extensive associated thrombosis and a correspondingly large region of the brain is robbed of its blood supply.

Septic emboli very promptly lead to gangrenous patches, multiple brain abscesses (metastatic brain abscesses) and death. Such cases often follow embolism dependent upon gangrene of the lung or septic endocarditis (Rothmann).

Embolic infarcts of the brain dependent upon *thrombosis of the pulmonary vein with pneumonia* offer a very grave prognosis.

The left middle cerebral artery is the most frequent seat of embolism. The area of softening includes the lenticular nucleus, part of the optic thalamus, the internal capsule—the great basal ganglia—with the cortex very often, because of the closure of the cortical branch of the middle or anterior cerebral arteries.

With embolism, the onset is sudden and the mental condition is clearer than with thrombosis or cerebral apoplexy.

Recovery is more complete with cerebral embolism than with thrombosis or with most apoplexies.

If the case becomes chronic, the symptoms of brain degeneration persist; the prognosis of all forms of occlusion or rupture (embolism, thrombosis and apoplexy) is practically the same.

Embolic infarcts of the brain are much less frequent than is cerebral apoplexy.

Lewandowsky reports 4 cases of embolism to 100 of hemorrhage.

Full and persistent loss of consciousness, coming on suddenly, attributable to embolic infarct, always offers an unfavorable forecast.

Cerebral fat embolism following fractures, often comminuted, operative interference, or other trauma, is always serious and usually leads to death in from 1 to 5 days after the beginning of cerebral symptoms.

Cerebral emboli breaking away from aneurismal coagulum often lead to prompt softening with consecutive disturbance of function and always offer a gloomy forecast.

Cerebral plugging with puerperal infection is always a grave accident and rarely mends.

Embolism causes more deaths among women than men.

Osler says that this is due to the greater frequency of mitral stenosis in women. Pitt, on the other hand, found that of 79 cases at Guy's Hospital 44 were males and 35 females. Saveliew reports 54 per cent in women.

Diphtheria and Hemiplegia.—With diphtheria, hemiplegia is usually of embolic and of endocardial origin; it is serious; rarely do the patients recover full use of the half of the body affected. Rolleston found in 9,075 cases of diphtheria (6) of hemiplegia; of these (4) died. In one of these there was an embolus in one of the cerebral vessels.

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(b) Cerebral Thrombosis

Thrombosis is more frequent than has been generally supposed; many cases formerly considered due to cerebral apoplexy are now known to be of thrombotic origin.

Pathologic conditions which predispose to cerebral thrombosis are all grave and include arterial degeneration—arteriosclerosis—infectious diseases, myocardial insufficiency, lowered systolic blood pressure, brain tumor, abscess, all diseases associated with cerebral pressure and obstruction of the sinuses of the brain—malnutrition and inanition.

The left cerebral vessels, as in embolism, are more frequently involved than are those of the right side. The deeper branches are oftener plugged than the more superficial, hence foci of softening result very often in the pons and in the medulla oblongata, a complication at once threatening and serious.

In many cases death follows before softening of the brain tissue has had time to develop. There are occasional cases in which both sylvian arteries are obstructed at the same time and a large part of the brain softens in consequence—always hopeless.

When the thrombus forms slowly and is small, the symptoms increase gradually, and the prognosis is more favorable, always depending, however, on the vessel involved.

In some cases of malnutrition, *multiple "marantic" thrombi* form, a large number of foci of softening resulting; the cortex is mainly involved and the prognosis of this condition (athrepsia—Parrot's disease) is always grave.

Primary thrombosis of the longitudinal sinuses is a condition found in young subjects, children oftenest, who are suffering from extreme weakness, or prostration—the result of malnutrition. Both the underlying conditions as well as the complication are dangerous, and death usually results.

Grave anemias and leukemias occasionally end with sinus thrombosis, also cancer and pulmonary tuberculosis.

Sinus phlebitis or thrombosis following otitis, usually suppuration, is as a rule, a serious complication, but *prognosis has been materially improved by early detection and radical surgical treatment* (See Surgical Treatises and the more recent Monographs by aural surgeons).

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When a thrombus forms about an embolus, symptoms are likely to increase, degeneration is progressive, and in most cases the prognosis is bad.

Thrombosis of any of the cerebral vessels *due to blood changes and weakened heart* usually leads to deep involvement of the sensorium, coma, and death.

Thrombosis associated with specific endarteritis (See Syphilis) often with hemiplegia, not infrequently shows very satisfactory results from rigorous treatment. In many cases there is a remnant of *hemiplegia* which remains uninfluenced by any treatment; often the mental condition of the patient is normal, though these subjects are without normal resistance; fatigue follows slight physical and mental effort while some remain permanently emotional, forgetful and below par in all respects.

In *senile subjects with arteriosclerosis, gradually increasing thrombosis leads to death* within a limited time.

Thrombosis of one or more of the cerebral vessels with *chronic alcoholism* is an occasional complication; "*wet brain*" is usually developed in these cases, and death is the result.

Cerebral thrombosis during the puerperal period with or without sepsis is always serious; usually fatal with sepsis.

Thrombosis of the vertebral or basilar artery may give rise to symptoms of pseudobulbar paralysis.

Thrombosis of small arteries may exist without giving rise to symptoms of any kind. Cases have been reported in which there were multiple but small thrombi with unchanged intelligence.

The prognosis so far as life is concerned, following the initial coagulum, is not as bad as with either cerebral hemorrhage or embolism.

Jones reports that death follows within the first 24 hours in 30 per cent of apoplexies, 15 per cent of thromboses, and 7.5 per cent of embolisms.

Coma is better and longer borne by patients with thrombosis and embolism than by the subjects of cerebral hemorrhage. If the coma deepens or is deep from the beginning, the prognosis is correspondingly bad.

The *condition of the cardiovascular organs* is of the utmost importance in the prognosis of cerebral thrombosis. Marked myocardial weakness is almost always followed by death.

Thrombosis with paralysis, hemiplegia bulbar paralysis, pneumogastric or phrenic involvement always offers a grave forecast. Unless the paralyses disappear within a few weeks, they are likely to remain uninfluenced. In all cases the location of the thrombus and the size of the focus of softening are of enormous prognostic significance.

The *mental condition* is better in embolism than in thrombosis as a rule.

Softening of brain tissue is as a rule more favorable for the continu-

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ance of life than is cerebral hemorrhage. The foudroyant cases are less frequent in which death follows within a few hours with embolism or thrombosis than with cerebral hemorrhage.

If patients live, the final damage to brain tissue is greater with softening (embolism or thrombosis) than from cerebral hemorrhage.

The *paralysis* due to brain degeneration (softening) is likely to be more persistent because of the complete destruction of tissue and the extension of the destructive process, than with hemorrhage.

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4. Cerebral Hemorrhage

Apoplexy (Cerebral)

General Considerations.—An escape of blood within the intracranial centers is but a symptom as a rule, of degenerative, and possibly complex conditions.

The diagnosis of cerebral apoplexy once established, the forecast, because of the pathologic conditions underlying, must always be guardedly given and the lesion should be considered of grave import.

Cerebral hemorrhage is evidence of diseased vessels and usually raised blood pressure, often associated hypertrophy of the heart, and in many cases vascular change in the kidney and other organs.

There are cases in which hemorrhage occurs without increase of blood pressure; it may be assumed, however, that *when disease of the cerebral blood vessels exists, increased blood pressure is the most active factor in causing cerebral hemorrhage.*

Associated Symptoms.—*High blood pressure, with symptoms of either incipient or advanced change in the cerebral vessels may be expected on slight cause to lead to rupture, with all of the attending dangers.* This is to be specially feared with the chronic changes mentioned above and associated *chronic nephritis with the usual hypertrophy of the left ventricle.*

Increased blood pressure may be associated with a number of condi-

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tions, but when present with hypertrophy of the left ventricle, particularly when there is broken compensation, the cerebral vessels are in great danger.

Cerebral hemorrhage is often associated with chronic interstitial nephritis. In these cases the lesions of both conditions resemble each other, for in both the arteries are sclerosed. Chronic granular kidney includes hypertension, and in most cases deep involvement of the cerebral vessels. Chronic interstitial nephritis cannot be divorced from arteriosclerosis, particularly of the cerebral vessels.

Many hemiplegias supposed to be due to cerebral hemorrhage are found on post mortem dependent on thrombotic softening; this is also true of the cases mentioned in the preceding paragraph, in which there is marked hypertension with positive clinical manifestations of granular kidney (Janeway).

Hypertension alone, without vascular lesions, is not sufficient to cause rupture of the vessels. The presence of miliary aneurisms with abnormally high systolic blood pressure and often an extra and sudden strain, are the factors which are paramount in causing the majority of cerebral hemorrhages (Charcot).

Arteriosclerotic processes may be largely limited to the cerebral arteries while changes in distant vessels may be so slight as to remain unnoticed, or the opposite condition may exist in which the cerebral vessels are spared and arteries of the extremities or other internal organs, as the heart, intestines, kidneys, and spleen, may alone show advanced degeneration. As a rule it may be assumed that with true cerebral apoplexy there are likely to be marked and advanced lesions in the heart muscle, its vessels, and the arterial tree.

The influence of sudden increase of arterial blood pressure, in the subjects of cerebral miliary aneurism following excitement, over-eating, sexual indulgence, muscular strain, hurry—under stress—worry, and often acute infection, alcoholism, and tobacco poisoning upon existing cerebral vascular degeneration is enormous, and is often responsible for hemorrhage.

The influence of the *sudden contraction of the cutaneous vessels* (after or during a cold bath or exposure) in the subjects of cerebral arterial degeneration, demands the closest consideration in framing the prognosis.

Patients with arteriosclerosis and fair-sized miliary cerebral aneurisms may, as the result of *increased venous pressure* (straining at stools, coughing, sneezing, laughing, during epileptic convulsions, women during labor, or whooping cough), rupture a small or large vessel in the brain. In these cases the veins are likely to be primarily diseased.

When cerebral hemorrhage is a complication of grave constitutional disease (*typhoid, puerperal fever, endocarditis, nephritis, purpura, per-*

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nicious anemia, leukemia, scorbutus, etc.) the prognosis is clouded, and is the more unfavorable because of the malnutrition of the vessels. In some of these complications the hemorrhage may be multiple.

Age.—Deaths from cerebral apoplexy are increasing, as is all arteriosclerotic disease, with the onward march of civilization and the stress of modern life. This is shown by the increase of cerebral apoplexy in young subjects. Until within the past three decades, death from cerebral hemorrhage was comparatively rare before the fortieth year of life, now while as before the arterial changes which underly the hemorrhage are largely dependent upon the habits of the individual, there is an increase in frequency with each succeeding decade.

I exclude from consideration the *traumatic cerebral hemorrhages,* which are numerous during the first years of life. Thomas offers the tables, condensed from the Census Report. "The estimated population

TABLE I. CONDENSED FROM THE CENSUS REPORT OF 1907.

DEATHS FROM APOPLEXY AND PARALYSIS

Decade	Cases	Proportion per 1,000 of Deaths
First	670	20.1
Second	121	3.6
Third	370	11.1
Fourth	998	30.
Fifth	2,250	67.7
Sixth	4,836	145.4
Seventh	8,491	255.3
Eighth	9,877	297.
Ninth	5,100	153.4
Tenth	544	16.4
Total	33,257	100.0

TABLE II. CONDENSED FROM THE CENSUS REPORT OF 1906.

Population of Registered States in 1907, Distributed According to Ratios Found in 1900		Deaths from Apoplexy and Paralysis in 1907	Liability per 100,000 Population	Relative Liability
First decade	6,984,883	670	9.6	5
Second decade	6,204,278	121	2.	1
Third decade	6,260,922	370	5.9	3
Fourth decade	5,171,628	998	19.3	10
Fifth decade	3,760,575	2,250	59.8	30
Sixth decade	2,550,957	4,836	189.6	95
Seventh decade	1,579,307	8,491	537.6	269
Eighth decade	734,016	9,877	1,345.6	673
Ninth decade	180,990	5,100	2,817.8	1,409
Tenth decade	13,406	544	4,057.9	2,029

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in the Registration States in 1907 was distributed among the decades according to the ratios found in the census of 1900, and compared with the number of deaths in each decade which were reported during 1907. The error introduced cannot be great. The relative liability in the different decades is expressed in proportion, taking the liability in the second decade as 1. The increase in liability with each succeeding decade is certainly striking."

Frequency is not to be confounded with liability to hemorrhage.

The prognosis in each decade is materially influenced by the etiology of the individual cases. During early life traumatism is an important etiologic factor.

The United States Census Report for 1906 shows that of 961 deaths due to apoplexy and paralysis, 882, approximately 92 per cent, occurred in the first 5 years of life. A large number of these were congenital.

The influence of *acute infections* during the first decade of life is paramount. *Spontaneous rupture of a cerebral vessel is unlikely in the child.* In the infections of early life, rupture is only possible when there are degenerative changes in the walls of the blood vessels. A fair proportion of these cases recover, leaving more or less damage.

During the first decade of life *infantile convulsions* are only occasionally followed by hemiplegia dependent upon hemorrhage. In these cases, particularly if epileptic, the paralysis when present is not likely to be due to hemorrhages but to other organic disease. Rupture of an artery during an epileptic convulsion is a rarity.

Hemiplegia following convulsions in young subjects is due in the majority of cases to acute encephalitis (Strümpell), to the cerebral type of infantile palsy, to thrombosis and embolism associated with the infections, to whooping-cough in which intracranial hemorrhages may occur, following great increase in venous pressure during paroxysms of coughing. All of these cases offer prognoses in accordance with the malignancy of the primary infection, the extent and character of the cerebral lesion.

Inflammatory changes in the brain, hemorrhage, thrombosis, and embolism during the first decade, rarely leave the brain undamaged—more or less permanent paralysis persists during life. A large number of these children die during the initial stage of the complication.

It is safe to conclude that in children with symptoms of hemorrhage, including paralysis, except in the cases of encephalitis and with positive evidences of infection, there is invasion of the vascular system and the prognosis is grave in consequence.

The infections include whooping-cough, typhoid fever, diphtheria and measles. Scarlet fever is rarely associated with hemiplegia (Rolleston).

Malignant endocarditis in early as well as in adult life, with embolic infarct leading to hemiplegia, is always fatal.

Hemiplegia due to hereditary syphilis in early life under proper treat-

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ment may recover with but slight damage; if neglected, secondary descending contractures and paralysis remain.

Hemorrhage with glioma early in life may hasten the end.

Infantile cerebral paralysis, whether hemiplegic or paraplegic, may be complicated by *posthemiplegic chorea, athetosis, or epilepsy. Developmental anomalies* are frequent and are never entirely overcome; on the other hand cerebral paralysis in the child may be severe, and yet recovery may follow without damage. The liability to apoplexy in the second decade of life is decidedly less than in the third. Statistics prove that there are fewer cerebral apoplexies between the tenth and twentieth year than at any other period during life. The factor of accident, including the birth palsies is largely removed.

As we advance to the third decade of life syphilis becomes an important pathogenic factor in cerebral hemorrhage and hemiplegia (See also Cerebral Syphilis). *Specific endarteritis with ultimate apoplexy* in cases recognized early and not too extensive, admits of successful treatment. In many of these cases, particularly in young subjects, I have had excellent results.

Cerebral hemorrhage, aphasia, and hemiplegia, complicating the puerperal period is always a serious complex. I have recently treated such a case, in which after several weeks, symptoms of renal calculosis developed; the stone was located by x-ray and successfully removed. The hemiplegic has made a fairly satisfactory recovery with but small damage. If in these cases (puerperal), *coma* is deep at once and the patient fails to react in from 36 to 48 hours, the prognosis is bad, and death follows after a number of hours of irregular breathing.

Patients with *endocarditis* between the twentieth and fortieth year not infrequently suddenly develop symptoms of cerebral apoplexy which are due to *embolic infarct* and in the majority of cases, if the latter is of considerable size or the pons or medulla are included, the prognosis is bad. *Non-malignant endocarditis* may be associated with infarct; paralysis may exist and yet restoration of fair functional ability may follow; death may result from intercurrent disease early or years after the paralysis.

So-called *"spontaneous cerebral hemorrhage"* in subjects before the fiftieth year is exceedingly rare, and when it is suspected demands close examination. In the majority of cases a lesion will be discovered which, as a rule, makes the forecast gloomy.

The larger number of cases of cerebral apoplexy demanding our attention are found in subjects between the fiftieth and seventieth years. It is during this span that arteriosclerosis plays a most important role.

Syphilitic hemiplegia due to *specific endarteritis* is less frequent after the fiftieth year than between the twentieth and forty-fifth years.

Monakow found that 0.9 per cent of the population of Canton Zurich died annually of apoplexy. Only 15 of 269 of these cases died before the fortieth year; 3.7 per cent of all deaths were due to cerebral apoplexy.

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Heredity.—*Family history* gives important prognostic data in many cases of cerebral hemorrhage. It is not unusual to find several members of a family yield to apoplexy at about the same age, with almost parallel symptoms; as a rule such cases are not likely to become chronic, but early death after a short period of hemiplegia and coma is the rule. When, after coma and hemiplegia these patients live, they rarely make recoveries which are satisfactory. Such patients may with hemorrhages into the internal capsule or other centers, live during periods of varying length—paretic and with but little of their original spirit.

In connection with the subject of heredity Monakow contends that "these children inherit a lowered resistance of their cerebral arteries," possibly a weakness of the intima, a tendency to aneurismal dilatations, a predisposition to diseases of other organs (kidney, heart, etc.) which invite arterial change.

Sex.—The census reports fail to show that sex is a factor of importance in causing cerebral hemorrhage. In hospital practice there is usually a preponderance of male deaths over the female.

Thomas in America, and Monakow in Switzerland have both reached the same conclusion, i. e., that *sex does not appear to have a marked influence.* Thomas reports that "among 1,000 of the aggregate population within the Registration States the proportion in 1900 was: 505.8 men and 494.2 women, while among 1,000 deaths from apoplexy and paralysis in 1906 there were 504.5 men and 495.5 women."

In my hospital service I find again as many men as women. Monakow found no noteworthy difference in his home (Zurich) in Switzerland.

Climatic Influence.—Hot weather, sudden changes—either excessive heat or extreme cold, the former more particularly—prove to be unfavorable to the subject predisposed to apoplexy. The prognosis of cerebral apoplexy in a plethoric subject, when stricken during extremely hot weather, is usually unfavorable.

Habitus apoplecticus.—*The influence of the apoplectic habit* on my material justifies the conclusion that the plethoric and obese subject, if he becomes intemperate in any of his habits, is more likely to develop degeneration of the arterial wall than are normal individuals. This subject, in spite of its age, is still *sub judice.*

Overeating, alcoholic excess and dissipation are all factors in reducing vitality and resistance, as well as changes in many organs with final degenerative changes in cerebral arteries and heart.

Given an apoplectic, obese and plethoric subject with the habitus apoplecticus, it is safe to conclude that in such a subject the chances of recovery or partial restitution are materially reduced.

Gout and rheumatism produce changes which invite arterial degeneration—hence cerebral atheroma and hemorrhage.

Cerebral apoplexy in subjects surcharged with lead is associated as a

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rule with marked cardiovascular and renal changes, which make the prognosis grave. *The combination of hemorrhage, uremia and plumbism* not infrequently leads to prompt death.

Occupation.—All occupations which include stress and hurry, which are sedentary and which require great physical force invite arteriosclerosis and consecutive apoplexy (See Arteriosclerosis and Occupation).

The Influence of Special Symptoms on Prognosis

Prodromata.—*In all cases, whatever the symptoms, the localization of the lesion in the brain and size of the hemorrhage remain the most important prognostic factors.*

Hemorrhages into the brain substance following a period of prodromata offer no different prognosis than do those cases in which the positive evidences of apoplexy are fully developed without a moment's warning. The prodromal symptoms of approaching hemorrhage which often include, besides vertigo, somnolence, nosebleed, high blood pressure with hypertrophy of the heart and positive evidences of chronic nephritis, may prove of advantage when correctly interpreted, for the warning leads to rational treatment and living which may postpone rupture of a cerebral vessel.

The early appearance of retinal hemorrhage with positive evidences of cerebral sclerosis, high blood pressure, heart and renal changes, made positive by physical signs, vertigo at times, occasional vascular spasm (cerebral), includes a symptom complex which argues unfavorably for the future. Only a small proportion of such cases live to have apoplexy; most of them die of cardiac or renal insufficiencies. When intracranial pressure is added, the prognosis in the majority of cases is bad and life is not easily prolonged. There are exceptions to this conclusion, but they are few.

The influence of symptoms on the prognosis of the average cerebral hemorrhage demands the consideration of—

(a) The apoplectic attack
(b) The period of reaction
(c) The period of paralysis.

1. *The Apoplectic Attack*

Coma.—In the majority of cases coma follows hemorrhage into the brain substance. *The deeper the coma, the graver is the prognosis in most cases.* While coma is *the* pronounced and the earliest symptom recognized as being most significant, there are but few cases in which other positive evidences of the presence of hemorrhage are wanting before there is loss of consciousness (Trousseau).

In some of these cases the cerebral hemorrhage may be so slight or

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so localized as to remain unnoticed by the patient, or by those about and with the patient. There are many small cerebral hemorrhages which give rise to but few or no symptoms, which are finally encapsulated or absorbed. Such cases may precede larger and fatal hemorrhage. Post mortem examination of large and promptly fatal hemorrhages often shows the presence of the remnant of previous small hemorrhages which caused no symptoms.

When during the early stage there are *convulsive movements,* the prognosis is bad.

Irregular breathing with coma early, is ominous.

Cheyne-Stokes breathing is the most notable example of pathologic abnormality in respiratory rhythm. It is always significant of deep invasion of the central nervous system except in early childhood, when it is often physiological. There are respiratory abnormalities which approach the Cheyne-Stokes breathing, in which there is gasping respiration, with nodding of the head, "the chin being thrown quickly upward at each respiration and falling slowly with expiration." Such breathing indicates approaching death. It is also found in the terminal stage of uremia, as well as in brain compression from hemorrhage or other causes.

Von Monakow in his exhaustive treatise on cerebral hemorrhage reports, after an analysis of a large number of cases, that coma is an accompaniment of hemorrhage which is near to the central gray matter of the third ventricle, the nuclei of the optic thalamus, and that it is less likely to be present when the white matter of the cerebrum is involved. Jones (quoted by Thomas) found consciousness lost when the hemorrhage ruptured into the ventricle. He found that there was coma in 85.5 per cent of such ruptures, "while in the non-ventricular hemorrhages the percentage of loss was only 69.4 per cent. These cases offer an unfavorable prognosis."

The duration and the depth of coma influence prognosis powerfully.

The average duration in favorable cases is short—from one-half to three hours. Monakow's experience is the same. Coma which persists beyond 24 hours is always serious, and the majority of such cases die within 48 to 72 hours. It often happens that patients recover from deep coma with gradual return to consciousness, though the sensorium may remain dull during a number of days or weeks. When patients fail to awaken from the coma, death may be postponed several days during which they remain completely unconscious, and with rapid and irregular, often Cheyne-Stokes breathing, the rattling (mucus) in the throat increases, the pulse grows more and more rapid and irregular, the face loses its color, the facies change entirely (at times are Hippocratic) and with increasing rise of temperature, at times *hyperpyrexia,* death results.

Evanescent paralysis of one extremity, or hemiplegia—paresis, with evidences of vascular spasm usually recurring with advanced arterio-

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sclerosis and as a rule, *high blood pressure,* is likely to lead to final hemorrhage with deep coma from which the patient rarely rallies. In some cases there may be short periods during which the sensorium is blunted, and there are *occasionally epileptiform seizures* before the final deep coma leads to death.

I have seen cases in which the vascular spasm or epileptiform attacks recurred during long periods (6 to 18 months) before the final deep coma due to hemorrhage developed. Many of these cases were found in nephritis (chronic interstitial nephritis).

PUPILS.—Extreme contraction of the pupils is characteristic of hemorrhage into the pons; the forecast is not encouraging.

The size and reactions of the pupils vary, and offer but little assistance in the majority of cases for prognosis. The pupils in serious cases may be of normal size, or they may be contracted, unequal or dilated. As a rule it is safe to hold that in the most serious cases the light reflex is abolished while in the milder cases the reactions continue, though they may be abnormally sluggish.

The sensorium during the attack is differently affected; its long disturbance is serious. Hemiplegia dependent on *hemorrhage without loss of consciousness* during the "attack" offers a very favorable outlook so far as life is concerned, in the majority of cases.

TEMPERATURE.—Temperature study is of great prognostic value.

Long continued *subnormal temperature* following outspoken symptoms is unfavorable. In most cases there is a fall of temperature (1°-2.5°) early, but for the favorable forecast this subnormal temperature should yield to a gradual rise of a few degrees within from 1 to 3 hours.

A long period of subnormal temperature with rapid, irregular, and small pulse is unfavorable.

Marked rise of temperature during the first 24 hours—*hyperpyrexia*—is found in the gravest cases and with deep coma, evidences of meningitis, these patients die within a limited period (12 hours to 2 or 3 days). The highest temperatures following cerebral apoplexy are suggestive of invasions of the pons or medulla oblongata.

The most favorable cases for continuation of life are those in which the fall of temperature has not been extreme, the reaction prompt, and the sensorium but slightly disturbed. Such cases often show complete hemiplegia just as do the more serious cases, and the return to approximate health may be as slow as in the cases in which the symptoms of the attack—early—were more threatening.

PULSE.—The pulse early in the attack is slow; it may fall to 45. The average case offers a full bounding pulse of about 60 per minute. With persistent collapse and finally rapid heart action the prognosis is unfavorable. With accompanying nephritis, the persistence of an abnormally slow and tense pulse after the first 24 hours is always ominous,

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for in the majority of cases, the blood pressure may continue high to the end, but the pulse will soon show the evidences of heart weakness; it becomes erratic, rapid and intermittent as well as arhythmic, and refuses absolutely to respond. The slow, tense, and bounding pulse is likely to show evidences of insufficiency if it persists as suggested above—beyond the average period.

Before death, in most cases, there are indications which include surrender of the heart before respiration is paralyzed, for the breathing continues during a limited time after the pulse ceases to beat. When the attack is rapidly fatal the respiratory and cardiac centers in the medulla are comparatively often involved. Such occurrence is not frequent. Even with previous hemorrhages and recurrence, sudden death is not the rule.

Acute Bed-sores.—The acute bed-sore which appears on the buttock of the paralyzed side is always a menace. It extends with surprising rapidity, is large and destructive, is associated with the septic state, and almost always leads to death. This acute bed-sore, fully described by Charcot, usually develops about seven to ten days after the development of hemiplegia.

An extensive erythematous blush over the buttocks early, particularly if there are vesicles present, is suggestive of acute bed-sore, and local gangrene may be expected.

Ophthalmoscopic Examination.—Ophthalmoscopic examination does not offer evidence which proves of material assistance in the prognosis of apoplexy; there are so many symptoms upon which a forecast can be based without the ophthalmoscope. Further there is the fact that it is not often at hand when desired during the attack, and that usually the average clinician fails to use it early in these cases. Knowledge of the condition of the blood vessels, however, may be gained by using the ophthalmoscope. By its use the interpretation of intracranial tension may be aided, retinal hemorrhage recognized and its influence on prognosis, which is not usually favorable, determined.

Duration.—Jones' table which was compiled from cases verified by autopsy is most instructive, for it gives evidence of the duration of the attack concerning which only an indefinite forecast can be given in the larger number of individual cases:

Lesion	Number of Collected Cases	Percentage Dying within 24 Hours	Within One Week	Within One Month
Hemorrhage.....	828	30.4	63.8	79.4
Thrombosis.....	158	15.8	38.0	74.7
Embolism.....	273	8.	35.	56.

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The average duration of early fatal cases may be placed between 7 and 10 days.

2. *The Period of Reaction*

The sooner the patient reacts the more favorable is the prognosis, provided the heart shows fair strength and the respiratory center is not profoundly involved. Reaction within 4 to 6 hours is favorable. The average period is between 24 and 48 hours.

There are unfavorable cases in which the sensorium is only slightly involved in which there is prompt reaction, possibly only slight delirium, and paralysis may be complete (hemiplegia) but the heart continues feeble, erratic and irregular. In from 18 to 36 hours the pulse becomes exceedingly rapid, the breathing irregular, and death follows within the following 24 to 36 hours.

Hemorrhage into the cerebellum and into the pons may not be associated with loss of consciousness, in the reactionary period; vomiting and collapse may, with feeble systolic force, threaten the life of the patient. Before and during the reaction the head and eyes may be turned in the same direction (Prevost conjugate deviation)—evidence of a severe condition. The deviation should always be interpreted as signifying grave danger; it is temporary as a rule, and is connected with a lesion of the lower parietal lobe.

Failure to react with increasing accumulation of mucus in the trachea and bronchi does not often yield, but with increasing stupor leads to death.

Return to consciousness, partial or complete, during the early days or hours, early during the period of reaction, and lapse into partial coma with respiratory involvement is always unfavorable and such patients usually show increasing evidences of compression from which they do not, as a rule, rally. In such cases the pulse may remain full and tense, and the systolic pressure comparatively high during several days, after which the break includes irregular breathing (Cheyne-Stokes) and final heart insufficiency, small, erratic and irregular pulse.

Rise of temperature with hurried or irregular breathing after reaction is always unfavorable. With *hyperpyrexia* during the period of reaction there is occasionally *glycosuria.* When this persists and the mind becomes clouded, as it often does with such complications, the outlook is not encouraging.

With tonic contraction of the non-paralyzed side, the suspicion of rupture into the lateral ventricle is justified, and as elsewhere suggested, such rupture is serious.

Convulsive seizures—either general or local, usually general—whenever present early or during the period of reaction, are evidence of irritation of the cortical region (motor area) and demand close consideration before their influence is finally decided.

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Retention of urine during the period of reaction or before, ought not to be considered unfavorable in most cases.

The involuntary loss of urine and feces in the first and second stage is more serious than retention, though many patients in whom there is loss of control finally improve. With a favorable mental condition the bladder and rectal functions return.

3. *The Period of Paralysis*

The hemiplegic who lives beyond the second stage of cerebral apoplexy is as a rule damaged, however favorable the course of the disease has been; he is often subject to subsequent attacks. This is the generally accepted dictum, but a strikingly large proportion of patients escapes second and repeated hemorrhages. Most hemiplegics are able to walk after a varying period. *The arm always improves slower than the leg, and the secondary contraction* due to descending degenerative changes (?) is, as a rule, more damaging and persistent in the arm than in the leg.

The exalted knee reflex is present in 92 per cent of all hemiplegias due to hemorrhage and is persistent (Ganault); rarely does the reflex become normal. When the knee reflex is not exaggerated during the period of paralysis, some complication should be suspected. In such cases Oppenheim found the presence of tabes in one, and cerebral tumor in another.

The prognosis is not unfavorably influenced by the presence or absence of the *Babinski phenomenon.* When late, it shows degenerative change in the lateral column. The absence of the *cremaster reflex* on the affected side is of no great prognostic significance.

Atrophy of muscles, the cause of which remains problematic, does not materially influence the outcome in the individual case. There are occasional cases in which the limb remains cyanosed, cold and edematous with contractures, in which a return of function is hardly to be expected.

In occasional cases in which for some reason—either central (focal) or peripheral (neuritis)—the extremities (usually the hand and arm) are painful, the suffering continues during long periods and in some cases never entirely disappears. The flexor muscles of the arm show greater tendency to resume their function than do the extensors.

Secondary contractures once fully established are likely to be permanent; improvement of muscle strength may follow so that the extremity often becomes useful. Contractures of the tendo achillis, resulting equinovarus particularly, leads to deformity which remains a persistent handicap.

The motor fibers are often separated from each other by the effused blood following the hemorrhage without being broken or destroyed; hence fair or even full function may often be expected after absorption of the

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blood under such conditions. It is possible, on the other hand, for restitution of function to follow the destruction of fibers in the direct motor tract following apoplectic insult. This is true of destructive hemorrhage into the internal capsule, or very often the radiating fibers.

In most cases the motor paralysis is associated with an increase of the reflexes in the paralyzed limbs. This is not unfavorable. The extent and duration of the paralysis must always depend upon the location and size of the hemorrhage and the condition of the brain tissue.

In the mildest attacks, in those cases which promise most there may be only a transitory vertigo, no loss of consciousness, no paralysis, severe headache at times, numbness of one extremity or one-half the body. In these "*transitory cases*" the return to a favorable condition is the rule. Such attacks may be repeated at short intervals, or after a period of prodromal symptoms there are in some of these attacks the fully developed symptoms of the more serious attack with ultimate hemiplegia.

While the majority of hemiplegias are preceded by symptoms—more or less profound—of cerebral disturbance, paralysis may develop suddenly without the clouding of the intellect.

Hemianesthesia depends on the invasion or destruction of the posterior third of the internal capsule and the optic thalamus when it accompanies hemiplegia, and does not *per se* influence the outcome materially. Exceptional cases show the sensory without the motor paralysis; in these cases the sensory fibers alone are involved.

There are cases in which *aphasia, hemiplegia,* and *hemianesthesia* are associated. As a rule, *hemianesthesia* does not persist long unless there is complete destruction of the posterior part of the internal capsule. Improvement may be long postponed, but in the end in most cases there is at least partial return of sensation with motor improvement, and later almost complete restoration, though some sensory disturbance may continue.

Hemiplegia which remains unchanged during three or four months following the initial hemorrhage is likely to persist until the end of the patient's life.

Improvement of motor function which begins within from three to six weeks after the insult, is likely to lead to almost full restoration of function.

There are cases in which years may lapse between attacks without material improvement, or there may never be a recurrence of hemorrhage in such cases.

Rupture into the ventricle is rare before the sixtieth year, but as already suggested, it is a grave condition.

Aphasia with hemiplegia due to cerebral apoplexy offers a relatively favorable prognosis so far as life is concerned. Speech in most cases returns, though the improvement is often discouragingly slow and the

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failure of the patient to express himself satisfactorily leads to marked depression; in those who are emotional this element becomes ascendent. In occasional cases complete aphasia may persist during the life of the patient. This is less likely to be the case with apoplexy than with *obliterating endarteritis of the cerebral arteries and associated thrombosis.*

A remnant of *aphasia* must be expected in a proportion of cases. The patient should in favorable cases, where there is even slow improvement, be encouraged to look for greater improvement ultimately—barring recurrence of hemorrhage.

The *prognosis of aphasia* with hemiplegia in young subjects is much better than in adults, and the child is often easily educated to speak by the development of the corresponding portions of the brain. In young subjects the compensatory power of the opposite hemisphere is often surprising, though at times the improvement may be slow. In the adult hemiplegia with aphasia offers a less favorable prognosis for restoration of function. As already suggested in some cases speech may never fully return, and if it does there is likely to be an apparent defect, the misplacing of words. The great irritability of the patient with the emotional element in the ascendency makes the patient exceedingly unhappy.

Re-education is possible in a proportion of cases. Many are taught successfully to write with the left hand.

Hemianopsia is likely to persist unless there is marked improvement within the first four weeks. Hemianopsia often disappears entirely within the first fourteen days. If the visual path at the sensory crossway is destroyed or injured, hemianopsia persists.

During the period of paralysis the contractures already mentioned develop (1 to 4 months). It occasionally happens that the contractures do not follow, and in rare cases, contractures which may have persisted during a number of years disappear with the appearance of extreme atrophy of the muscles. This condition follows secondary lesions in the trophic centers of the cord.

Contractures once fully established are not likely to disappear.

Any evidence at any time of inclusion of the *medulla oblongata* at once demands an unfavorable prognosis. *This includes glycosuria with respiratory and circulatory symptoms.*

Transitory albuminuria with symptoms of disease of the medulla is ominous.

Swellings of the joints (*arthritis*), *edema of the arm and hand* with, at times, *excessive sweating and increasing contractures of the fingers and hand* are symptoms which usually persist; they are exceedingly annoying and are not influenced materially by treatment.

Among the posthemiplegic motor complications are rhythmic contractions, irregular, at times sudden, contractions of the paralyzed extremity and athetosis.

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With these symptoms the motor paralysis is not complete, and as Church and Peterson contend "their presence implies a condition of irritation somewhere in the path of the upper motor neuron. This is usually furnished by lesions in the region of the basal ganglia, especially those affecting the optic thalamus and impinging upon the capsular fibers."

Posthemiplegic chorea does not often complicate hemiplegia in the adult dependent on hemorrhage. The movements may be continuous or accompany movements in connection with voluntary motions of the paralyzed, occasionally of the unaffected, side.

Hemorrhage into the anterior lobe and into the centrum ovale of considerable size without lasting symptoms is not impossible. Hemorrhage into the posterior lobes of the brain is likely to leave disturbances of vision and remnants of aphasia.

Mental Condition Following Cerebral Hemorrhage

In the majority of cases in which there has been deep coma during a limited period, return to full consciousness may require several days, often longer, during which time the patient does not fully appreciate his condition nor is he entirely conscious of his surroundings. He may, if aroused, be able to answer questions of minor importance intelligently, but any mental effort requiring thought will as a rule prove to be impossible. This conclusion holds for the majority of cases, but there are exceptions depending naturally on the extent and location of the lesion and the rapidity of the absorption of the effused blood.

In those cases in which the mental condition does not improve with the motor paralysis, careful inquiry into the previous mental condition of the patient should be made. In a large number of such cases the advanced arteriosclerotic condition of the cerebral vessels had, before the hemorrhage, produced positive evidences of mental deterioration.

Hemiplegia may never be associated with mental anomalies in occasional cases. In mild attacks there are no apparent mental after effects.

A large number of hemiplegics continue emotional during long periods, though some of these, in spite of a persistence of partial paralysis, must be credited with testamentary capacity; they assume responsibility and display good judgment.

Dementia fully developed following cerebral apoplexy is dependent upon cerebral softening (encephalomalacia). Oppenheim believes that this complex rests upon "general atheroma and more particularly follows apoplectic insult which is of syphilitic origin."

"The power of intelligent attention suffers most in damage from any cause to the prefrontal lobes" (Robertson).

Change of disposition is not infrequent; idiosyncrasies may develop and yet judgment may not be impaired. The larger number of deep

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apoplexies which improve or in which there is a return to approximate health will show some enfeeblement of mental power.

Repeated hemorrhages weaken the intellect; there is increasing feebleness of mind and body in most of these cases. Finally with inability to move about, bladder and rectal control is lost in the terminal stage, and the end is not long postponed.

In young subjects during the early days of apoplexy the mental symptoms may be prominent; these are likely to yield with the general improvement of the patient. In many, during long periods, the memory for remote events is fairly well retained while recent occurrences are promptly forgotten.

Maniacal disturbances sufficient to justify commitment may occasionally develop after cerebral hemorrhage. The duration of such a condition is not long as a rule—varying from two to four weeks, rarely longer. Relapse is possible usually after from two to four weeks.

Cerebral apoplexy in the insane may be followed by a striking change in the patient; it has been noted that the noisy and troublesome are often more quiet and more easily controlled than before the hemorrhage. The mental status of the insane patient is lower, as a rule, after the hemorrhage. With general paresis, the hemorrhage is usually of sufficient size to cause deep coma and death in from twenty-four to seventy-two hours.

Large hemorrhage into the internal capsule may exist without symptoms referable to the mind.

Special Considerations

In planning the life of the subject of cerebral hemorrhage who has gone beyond the acute period, the clinician should remember the great likelihod of recurrence. The underlying and serious degenerative arterial disease cannot be overcome when once established; the slightest initial hemorrhage may be followed by a more serious and promptly destructive insult.

During the attack and during the period of reaction pneumonia may develop and lead to death within from thirty-six to seventy-two hours; rarely is the end long postponed.

Pneumonia is of all complications the most serious after cerebral hemorrhage. Once the patient finds himself beyond the acute attack and in the stage of reaction, even after he may be said to be convalescent, inflammation of the lung is a menace which threatens the patient; it claims a large number of victims.

The average duration of life of the hemiplegics has been in my experience between five and six years. I have never yet found a case which proved to my satisfaction that cerebral apoplexy was in any way a conservative measure, or that the enforced rest which followed the

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"shock" was of material value in preventing "arterial strain," or that life was thereby prolonged.

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5. *Encephalitis*

(non-suppurative)

(*Acute and Chronic Encephalitis, Acute Hemorrhagic Encephalitis*)

Encephalitis may be considered a symptom complex due to infection, usually secondary, in which there are foci of inflammation throughout the brain, in the majority of cases accompanying hemorrhagic deposits, often due to infarcts.

Pyogenic cocci may cause either the suppurative or the non-suppurative variety of the disease.

Ernst has demonstrated the occurrence of encephalitis following traumatism, cases due to metastases and a class of infections which spread from neighboring inflammatory foci; most of these are conveyed through the lymph stream. The cases of encephalitis of hematogenous origin or those which spread by contiguity, show the primary changes in the connective tissue and blood vessels.

Encephalitis secondary to the acute infections (acute polyarthritis, cerebrospinal meningitis, typhoid fever, scarlet fever, erysipelas, measles, diphtheria, influenza, rabies, pyemia, splenic fever and endocarditis) is usually of the hemorrhagic type; it is often associated with large embolic infarcts, is of grave import and always materially increases the dangers

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of the primary infections. The strength of the patient has already been wasted and the resistance is low; the prognosis is correspondingly bad.

The larger number of encephalitides associated with hydrophobia, pyemia, malignant endocarditis and splenic fever are hemorrhagic. In all of such cases the prognosis is bad.

The prognosis naturally depends upon the size of the hemorrhage (infarct) and the malignancy of the primary infection. All sizes of hemorrhages occur.

In the chapter on typhoid fever, attention is called to the bad effect of hemorrhagic complications. There are epidemics of typhoid fever in which the hemorrhagic tendency is overpowering, and in which non-suppurative encephalitis is frequent and often fatal.

Cure is not impossible in these hemorrhagic cases, for the infarcts may be—usually are—circumscribed, may be absorbed or may lead to more or less *sclerotic change* in the process of repair. *Healing of hemorrhagic encephalitis with the formation of a cyst and focal symptoms* may follow within a reasonable time (6-10 weeks) in occasional cases. With such conditions cerebral localization is often possible and surgical interference, when the cyst is superficial, is successful in a small proportion of cases. The surgical treatment of the more *chronic cases* is less likely to be successful because of the permanent disorganization of brain elements, leukocytic infiltration and productive changes, cellular deposit and vascular growth (Ernst).

Acute encephalitis, a frequent complication of *influenza*, adds an element of great danger. In some of these cases the influenza bacillus has been found in the brain substance (see below).

Traumatic encephalitis (non-suppurative) may follow without break of the overlying tissues; disseminated encephalitis, without abscess formation, may also develop with middle ear and nasal infection (after nasal operations); with both of these conditions the prognosis is bad in proportion to the extent of the process—it is never to be lightly regarded.

There is a larger number of cases than is generally supposed in which the meninges are also involved (*meningo-encephalitis*). In these cases the clinical picture and thoroughly considered history lead to the suspicion of the complex character of the secondary infection; the Kernig symptom is present in over ninety-five per cent of the cases and the deep involvement of the sensorium after a period of indefinite symptoms depending upon the localization of the encephalitic foci must be regarded as being exceedingly serious.

Rothmann mentions the possibility of the association of encephalitis (non-suppurative) with small brain abscesses; the surrounding tissue is usually involved. If the abscess is not deep-seated, old or large, and is within reach of the surgeon's knife, the encephalitis yields with free drainage of the abscess.

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Suddenly arising cases with grave constitutional infection, hyperemia, early and mental torpor increasing to coma, are conditions which justify only the gloomiest prognosis.

Evidences of *multiple encephalitic foci* with increasing evidence of meningeal involvement or with high fever, rapid and irregular pulse—Cheyne-Stokes breathing—are found in the more serious cases.

Occasional cases show marked improvement during periods of remission and in spite of several exacerbations, recovery may finally be complete and permanent. Rothmann calls attention to this frequent favorable behavior of *influenza hemorrhagic encephalitides.*

In cases which live, in which during the acute or subacute period paralyses were prominent, there is rarely complete restoration of motor function. This is particularly true of the encephalitis of early life, which it may be safely concluded is responsible for many permanent paralyses (hemiplegia) and other serious complications including epilepsy (See Cerebral Palsies of Childhood).

The cerebral type of poliomyelitis (infantile paralysis) should be considered to be polioencephalitic. The majority of children stricken succumb to the disease. The prognosis is worse in those cases in which there is prompt loss of consciousness. In the severe, usually fatal cases, the loss of consciousness is sudden and complete. It is exceedingly difficult to differentiate from postbasic or other forms of meningitis save by lumbar puncture. Paralysis of the respiratory and glossopharyngeal muscles develops in the more serious cases, often hemi- or monoplegia before death.

Lumbar puncture offers no data which influences prognosis, though it assists in the diagnosis. These cases are fully considered in the chapter on infectious diseases (poliomyelitis).

Polioencephalitis (acute) Superior.—Wernicke called attention to the acute encephalitis of alcoholic origin in which there are well defined cerebral symptoms, much like those of influenzal origin to which I have above referred.

The delirium, cephalalgia, and somnolence are often associated with paralysis of one or more of the cranial nerves, usually the motor oculi. Strümpell mentions the occurrence of nystagmus and complete bilateral ophthalmoplegia. The association of alcoholic multiple neuritis in hospital practice is comparatively frequent. These cases rarely recover.

Respiratory paralysis with increasing heart weakness (rapid uncontrollable heart) with deep coma leads to death in from one to three weeks in the majority of cases, though an occasional case may recover after weeks of symptoms.

Psychic disturbances may persist during many weeks in cases which finally clear entirely; on the other hand, recovery with permanent mental defect and remnant of paralysis is also possible—and not unusual.

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Cases in which with either polioencephalitis superior or inferior, bulbar symptoms develop, may follow the Landry symptom complex. These cases should be considered polioencephalomyelitic. Their pathogenesis is similar to that of poliomyelitis; occasionally they have been traced to the influenza bacillus. The prognosis is bad.

Acute Encephalitis following Arsenical Poisoning.—Mentberger calls attention to *acute hemorrhagic encephalitis following the injection of salvarsan.* He insists that the fatal complication is due to arsenical poison which suddenly overwhelms the brain, promptly causes characteristic symptoms of encephalitis hemorrhagica without warning (cyanosis and edema of the face, clouding of the sensorium, vomiting, diarrhea, dyspnea, hiccough, pupillary paralysis, tonic and clonic spasms, final collapse and coma). Age nor sex seem to influence this complication though there is a decided predilection for young subjects, those without previous lesions of the brain or cord. It is further held that the complication may follow in any stage of syphilis, regardless of the dose of salvarsan injected. The complication may folow either the first or any subsequent injection. The encephalitis may develop within a few hours or several days after the injection.

The minority of those who have suffered from this form of encephalitis recover. The length of time during which symptoms persist is variable. Mentberger insists that the majority die, and that the deaths are most frequent among those who have appeared strongest.

In a large experience with salvarsan and the study of the material of many large hospitals I have failed to find experiences which parallel those of Mentberger. (For a full consideration of the subject of encephalitis due to salvarsan the reader is referred to the literature included in the work of Mentberger, also Fisher, Almquist and Oppenheim. See references.)

Polioencephalitis (*inferior*) is limited to the floor of the fourth ventricle and is fully considered in the chapter on *bulbar paralysis.*

Primary acute hemorrhagic encephalitis occasionally develops. Thorough search, as a rule, proves the process in the majority of cases to be secondary, but that there are unexplained cases which Strümpell believes justify their consideration as primary cannot be denied. In some of these cases the onset is acute; there is high fever and cerebral symptoms, delirium, stupor, severe headache, at times focal symptoms, aphasia, hemianopsia and evidences of cortical involvement. These symptoms may persist during several weeks or only a few days, after which there is improvement. But few symptoms persist during a varying period without progression, finally to disappear in most cases. Strümpell has called attention to the presence of "a marked optic neuritis with more or less marked venous congestion." There are some cases which lapse after a

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period of improvement. In occasional cases sudden and unexpected death occurs.

Lumbar puncture offers no data which influence the prognosis of any form of encephalitis.

6. *Cerebral Paralysis of Childhood*

(*Spastic Infantile Hemiplegia* (*Benedikt*), *Cerebral Paralysis of Children, The Acute Encephalitis of Children, Spastic Diplegia—Paraplegia*)

The Cerebral Paralyses of Childhood include:

(a) Paralysis due to intra-uterine anomalies

(b) Birth palsies

(c) Acute encephalitis of children—Spastic infantile hemiplegia (Benedikt).

(a) Paralysis Due to Intra-uterine Anomalies

Whatever the variety of paralysis due to congenital defects of the brain, the prognosis must be considered to be unfavorable. Faulty and arrested development is the most frequent cause, though intra-uterine hemorrhage or thrombotic softening are also factors.

The development of cysts during fetal life and resulting paralysis offers no hope for the relief of the resulting paralysis.

Arrest of development of the cortex cerebri is as a rule a disseminated process involving both hemispheres with resulting paralysis, which cannot be influenced by any known means.

The majority of children who are born with cerebral defects die early or are helpless with crippling contractures and mental weakness (idiocy). But few of these children live beyond the third year.

A large number of children who live beyond the third year also develop epilepsy. Cases in which there are convulsions early in life are not likely to live long. A long continued period of mental lethargy presages idiocy if the child lives. When with the cessation of convulsions the child brightens, the prognosis is correspondingly better.

Forty-five per cent of all infantile cerebral palsies develop epilepsy. "This occurs furthermore in about 50 per cent of the cases of hemiplegia, about 30 per cent of all forms of diplegia, and 36 per cent of paraplegias."

The Influence of Heredity on the Production of Epilepsy after Infantile Cerebral Palsies

Pierce and Sharp have offered some very interesting data bearing on this subject.

Cerebral palsies are oftener followed by epilepsy than is generally

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supposed. The question arises in the study of the cerebral palsies whether the individual case is likely to be followed by epilepsy. The severity of the paralysis does not seem to be a factor in causing epilepsy, for the investigation of the material at the Craig Colony proved that the mildest cases are often followed by the most severe epilepsy. The influence of heredity in epilepsy following infantile cerebral palsy is, as in so-called "idiopathic epilepsy," the leading factor. In 443 cases of cerebral (infantile) palsies with epilepsy complicating, compared with an equal number of cases of ordinary epilepsy the influence of heredity was the same in both forms.

In both, heredity proved to be a factor in approximately 70 per cent of cases, and in both alcoholism, mental disturbances and the neurotic constitution are of equal pathogenic significance in the offspring.

In the prognosis of cerebral (infantile) palsies therefore, heredity must be considered the most important factor. Cases with a family history of epilepsy are more likely than are others to develop the complication.

(b) Birth Palsies

Intra partum insult is the most frequent cause of birth palsies.

Premature birth, compression of the head in a narrow pelvis, twin births, asphyxia, hemorrhages due to constriction, cord constriction and forceps pressure are all factors which lead to meningeal hemorrhage invading the motor area of the cortex (Sarah McNutt and Cushing).

It is not always possible to differentiate the acquired and congenital paralyses at birth or later, for the symptoms of both may be the same and conclusive data may be lacking. The congenital or birth palsies during the first years of life are progressive. Unless there are associated disturbances which cause early death, the child as a rule learns how to walk much later than the normal time while speech development is also tardy.

In the cases of the "Oppenheim-Vogt type" the non-paralyzed side becomes rigid, and motor weakness is developed while athetosis is also prominent. The cases are known as a "*spastic diplegia*" (Diplegia spastica infantilis).

The intelligence of these children is not disturbed as a rule, and they may grow to manhood with characteristic contractures and facial expression, with persistent athetosis and unchanged spasticity. The associated symptoms are interesting; they include dislocation of the jaw, which is recurrent, bulbar symptoms, with, in occasional cases, inability to hold the head upright. Such children as they grow older are easily frightened by the slightest noise.

Freud classifies the cases of diplegia among the birth palsies to which Oppenheim agrees. Such diplegics live without increase of symptoms

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after they mature, are handicapped by their contractures, athetosis and motor weakness, and usually die of intercurrent disease.

(c) Acute Encephalitis of Children

Spastic Infantile Hemiplegia (Benedikt)

There is a definite form of hemiplegia which is found in children between one and four years of age which is dependent upon encephalitis which is hemorrhagic and acute. In the midst of apparent health the child develops high fever, lassitude and malaise. There may be a short period of nausea and vomiting; in the severe cases repeated convulsions are followed by prompt coma. The convulsions may be followed by paralysis without the development of coma, or the hemiplegia may not be recognized until the child brightens.

Improvement of the constitutional symptoms is prompt, but the paralysis, while it improves materially, does not entirely disappear. The arm, as the child recovers, is worse than the leg. Permanent trophic changes follow; there is arrested development, and in the most favorable cases there is among the remnants of symptoms some loss of motion.

Contractures are more or less developed in all cases with exaggeration of the patella tendon reflexes. There is rarely paralysis of any of the cranial nerves, neither do sensory symptoms develop save in occasional cases; there is some blunting of the touch sensation, and with closed eyes the ability to differentiate objects is lost.

In a number of cases of hemiplegia, *epilepsy* finally develops; the attacks may be either of the large or small variety and do not yield permanently to any form of medical or surgical treatment.

Athetosis is frequently present and remains a permanent symptom. *Chorea* is another refractory complication.

Speech defect is frequent; *mental development* is often retarded, but in many hemiplegic children the mind is bright and normal, though a limited number of these finally develop epilepsy. *Idiocy* is to be feared as is a *perverted moral sense.*

Sachs and Osler both contend that hemorrhage and embolic infarct are responsibile for the majority of hemiplegias of early life.

Aphasia with hemiplegia in the hemorrhagic form of encephalitis early in life disappears as a rule.

Patients with remnant of paralysis after hemorrhage during early life may reach old age.

Hereditary syphilis may prove to be the cause of hemiplegia in the child.

The infectious diseases of early life are occasionally associated with hemiplegia (measles, scarlet fever with nephritis, endocarditis, whooping-cough and smallpox). These cases are either embolic or hemorrhagic.

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The prognosis depends upon the nature of the underlying infection and the amount of injury to the brain, as well as the location of the lesion.

Choreic Paresis

There are cases of infantile cerebral paralysis in which the paralysis is not prominent but the symptoms develop gradually with *chorea and athetosis in the ascendency.* Freud has characterized these cases as "*choreic paresis.*" These cases do not often develop before the third year of life, and rarely after the sixth.

There is no danger of the development of *aphasia, epilepsy* or *dementia—contractures are not prominent. Chorea and athetosis are the leading symptoms.* Londe reports the case of a woman who was fifty years of age and who had this type of the disease since early childhood (spastic-athetotic).

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7. *Abscess of the Brain—Suppurative Encephalitis*

Abscess of the brain or *purulent encephalitis* is always of infectious origin, either secondary to aural disease, traumatism, or pus deposit in distant organs—one or more—and is rarely due to direct infection of the brain through the blood stream. It is safe to conclude that the so-

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called idiopathic abscess of the brain does not exist, and when it is strongly suspected thorough search will ultimately reveal a focus which may have given rise to neither subjective nor objective symptoms, may have been hidden during the lifetime of the patient, and may have been either acute or chronic.

The brain often tolerates the accumulation of pus during surprisingly long periods, either single or multiple; death in such cases may follow acute symptoms in a comparatively short time. A few hours or a single day have sufficed. Pus accumulation in the substance of the brain, unless it is given free exit, is always a menace and will in the end destroy life.

The bacterial infections which are responsible for the majority of infections which finally lead to brain abscess are either the streptococcus, staphylococcus, the influenza bacillus, bacillus typhosus, pneumococcus, the meningococcus, and the tubercle bacillus. The staphylococcus viridans is also included. Actinomycotic abscesses are occasionally found in the brain.

Naturally the prognosis is materially influenced by the location and the primary cause of the abscess. Ernst insists that 70 per cent of all brain abscesses are of local origin, and of these 24 per cent follow traumatism, and 42 per cent aural infections. Distant factors causing *hematogenous metastases* are prominent in 15 per cent, and in about 10 per cent of all cases the causes remain unrecognized. Seventy-five per cent of all cases are found in men while abscess due to traumatism is five times more frequent in the male than in the female. Abscess due to aural infection is again as frequent in man than in woman.

Jacobsohn's classification of brain abscess seems fully justified for our purposes with but one addition, for it is based upon the data offered in the preceding paragraphs and includes all clinical pictures of the disease.

Jacobsohn considers:

(a) The Traumatic Abscess of the Brain
(b) The Otitic Abscess of the Brain
(c) The Metastatic Abscess of the Brain

to which I add

(d) Rhinologic Abscess of the Brain.

Tuberculous abscess of the brain is considered in the chapter on tuberculous meningitis; its prognosis is always bad.

(a) Traumatic Abscess of the Brain

The traumatic abscess of the brain may develop without a break in the overlying soft or hard tissues. Contusion may be sufficient. An open wound of the soft tissues, without fracture, may suffice to give rise to

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fatal suppuration of the brain substance, to either single or multiple abscess, with or without *purulent leptomeningitis* (see Purulent Leptomeningitis). In occasional cases traumatism may not cause symptoms of abscess of the brain until weeks or months after the injury. In some of these cases there are suddenly arising symptoms; the entire course of the disease becomes fulminating, and unless there are focal symptoms or other features which lead to localization of the pus deposit and early surgical relief, death promptly follows. In another class of cases the development of the abscess is gradual, the symptoms positive, and with their increase the diagnosis becomes comparatively easy though exact localization may not always be possible. Exact localization either before or during operation which justifies drainage will succeed in saving over fifty per cent of these patients.

Cases which develop immediately after injury (fracture, contusion, etc.) are often complicated at once with purulent leptomeningitis; they involve the sensorium, develop the Kernig symptom, show characteristic changes in the fluid removed by lumbar puncture, and are less favorable than are the uncomplicated cerebral abscesses due to traumatism.

Bergmann contended in his classic treatise that "simple contusion of the scalp or soft tissues never leads to brain abscess." The majority of clinicians, medical and surgical, do not subscribe to this conclusion. In the consideration of this subject for purposes of prognosis I grant, as already suggested, the possibility of infection leading to brain abscess without discoverable break of the tissues but recognize that in the large majority of cases there is an open and demonstrable wound primarily.

Stab and gunshot wounds are among the leading causes of traumatic brain abscesses (Bergmann, Bruns, Oppenheim, Macewen); both may lead to multiple deposits with leptomeningitis. In these cases the prognosis is bad.

In many cases of traumatic abscess of the brain the abscess is superficially located and easily reached (often cortical).

The cases in which there is a long interval between the injury and the development of symptoms of abscess are less favorable than are those cases with frank and fully developed local symptoms immediately or soon after the injury. In the former cases the pus deposit is often deep seated and beyond the reach of the surgeon. In these cases the symptoms may not permit of localization; suddenly arising meningitis is occasionally the first suggestion of the presence of a lesion.

(b) The Otitic Abscess of the Brain

Suppurative disease of the ear furnishes the focus for over 42 per cent of all brain abscesses. The majority of these otitides are chronic and the infection extends as a rule through the tegman tympani to the

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temporal lobe, or from the mastoid cells to the cerebellum. In most of these cases there is also perforation of the tympanic membrane..

The abscess almost always develops on the side of the primary infection.

With *double otitis media suppurativa* I have found mastoiditis and abscess of the brain on both sides at the same time. In one of these cases the symptoms of pus accumulation were limited to one side and yielded to surgical intervention. The deposit on the opposite side gave no evidence of its presence during twelve months, when without previous symptoms or warning fulminating purulent leptomeningitis developed, ending the life of the patient in three days.

Jacobsohn's statistics prove that the abscess is located in the temporal lobe or its neighborhood four times as often as in the cerebellum.

Jansen offers the encouraging data which show but 7 abscesses of the brain in 5,000 cases of otitis.

Heiman found that of 570 otitic abscesses of the brain, 457 were due to chronic and 113 to acute aural suppuration. He further reports 456 abscesses in the cerebrum and 188 in the cerebellum.

Hegner found in 5,000 cases of chronic otitis in the Heidelberg Clinic, 17 abscesses of the cerebrum and 6 of the cerebellum.

Dench found that among 100 cases of cerebral abscesses 20 followed acute otitis.

Caries of the temporal bone following otitis media and the final development of *brain abscess with leptomeningitis* are among the graver complications, and offer a gloomy outlook.

In considering the effect of otitis during early life the clinician should remember that neglected cases may remain without symptoms for years, and that they may lead to brain abscess after puberty, though the discharge from the ear may have ceased, and that persistent *and neglected otitis with discharge may infect the brain years after its first appearance. Chronic and encapsuled pus deposit between the dura mater and the bone* may remain without symptoms during unlimited periods, but finally such accumulation is (in most cases) followed by brain abscess—either single or multiple—and unless promptly relieved ends in death.

The possibility of the occasional abscess formation on the side opposite to the primary otitis should be borne in mind. The prognosis is good in such cases if the abscess is recognized early and radical treatment is instituted.

With diabetes mellitus and otitis media with caries of any part of the temporal bone and brain abscess—an occasional association of lesions —the prognosis is absolutely bad.

With sinus phlebitis which is extensive, brain abscess may develop at a considerable distance from the primary lesion.

Otitic brain abscess is usually single, rarely multiple; this fact with

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its early recognition makes a favorable forecast possible in many cases. Between ten and fifteen per cent of abscesses of the brain following ear disease are multiple.

Perforation of otitic abscesses of the brain through the nose, ear, or through the temporal bone, is not frequent. Occasional rupture into the ventricle may cause sudden death, or rupture, which involves the meninges, may cause rapidly fatal meningitis.

Pyemia from aural and brain abscess occasionally develops; in these cases the prognosis is often doubtful during a limited period. The tendency to multiple pus deposits and the effect of general infection always make the prognosis grave.

Ophthalmoscopic examination often shows optic neuritis and choked disk. In the majority of cases the background of the eye remains unchanged. Ocular changes with abscess may occasionally lead to blindness. Compared with tumor of the brain changes in the background of the eye in abscess are much less frequent.

With otitic as with all other abscesses of the brain slow pulse early with increasing rapidity, arhythmia, and erratic behavior of the heart with or without respiratory irregularities are always of serious significance. The addition of Cheyne-Stokes breathing is not frequent but is always serious.

Focal symptoms even with large otitic abscesses of the brain may be absent, or there may be but few. In the majority of otitic abscesses the left temporal lobe is involved, and sensory disturbances of speech are often present persisting until the abscess is drained.

With *sensory aphasia, word blindness* may occasionally develop.

The *focal symptoms* naturally develop in accordance with the location and size of the lesion. *Abscess in the occipital lobe and angular gyrus,* as a rule, leads to *hemianopsia,* though abscess of this region (Rothmann) may develop without visual disturbance.

With *cerebellar abscess, ataxia* is a prominent symptom.

With marked *pressure on the direct pyramidal tract in the pons and medulla* there is hemiplegia with a spastic condition, exaggerated reflexes, and Babinski.

The *presence of paralysis of one or more of the cranial nerves* aids *in localization;* the prognosis is exceedingly grave in most cases in which, with basilar pressure, such paralysis exists.

Bulbar symptoms with brain abscess are evidence of disease of the pons and medulla and are always serious.

(c) The Metastatic Abscess of the Brain

The prognosis of the metastatic abscess of the brain is invariably grave; a large number of these are multiple and the primary disease is always threatening.

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The majority of the metastases to the brain from distant infection are embolic and develop on the left side, within the domain of the middle cerebral artery.

Among the infections which lead to metastases are *purulent diseases of the lung, bronchitis, empyema, abscess, and gangrene.*

Nather found 8 cases of brain abscess in 100 cases of pulmonary gangrene.

Pyemic and septic infection, ulcerative endocarditis may develop brain abscess, with or without focal symptoms; the deposit may be unsuspected. In all death follows within a limited time.

Brain abscess with pneumonia or a sequel of the disease is usually fatal.

Claytor gives the report of 58 cases of brain abscess following lung infections, of which 20 were associated with bronchiectasia, 10 with empyema, 9 with purulent bronchitis, 7 with gangrene of the lung, 6 with tuberculosis, 3 with pulmonary abscess, and 2 with pneumonia.

Brain abscess with any of the many distant infections other than those above mentioned, including malignant carbuncle, appendicitis, liver abscess, suppurative arthritis, osteomyelitis, uterine phlebitis and septic endometritis, dysentery, and ascending genito-urinary infection unless limited, with focal symptoms sufficient to make early diagnosis possible and with a good general condition and unusual resistance, offers no hope of relief by any known method of treatment.

(d) Rhinologic Abscess of the Brain

Brain abscess following nasal operations or spreading from nasal infection may develop without focal symptoms, or may be associated early with basilar purulent leptomeningitis. My experience with brain abscess following nasal infection has been exceedingly discouraging; the majority have died with symptoms of meningitis within from seven to ten days.

Caries of the ethmoid or other nasal bones, erysipelas, infection after removal of polypi and orbital phlegmon are among the primary causes from which the brain abscess may develop.

Brain abscess may occasionally follow tonsillar infection or operations for adenoids or other nasopharyngeal operations.

Parry reports such occurrence after the operations mentioned, and after septic disease of the eustachian tubes. The prognosis of these cases is based upon the same data as are paramount in reaching conclusions in the other forms of brain abscess.

There are *cases of brain abscess without known primary cause.* These are almost uniformly fatal. They are occasionally met during epidemics of cerebrospinal meningitis, and are probably due to the meningococcus of Weichselbaum.

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Conclusions.—Clinicians are agreed upon the following conclusions:

Brain abscess is almost always fatal unless relieved by surgical means.

Over 50 per cent of traumatic and other abscesses of the brain are saved by prompt localization and drainage. *Metastatic and rhinologic, as well as abscesses of unknown origin, offer an unfavorable prognosis in the majority of cases.*

Multiple brain abscesses are uniformly fatal. Surgery offers no encouragement in these cases.

Metastases to the brain due to septic processes may be present (as a rule the lesions are multiple) without symptoms, either general or focal; but such deposits hasten the end.

Pressure, edema, hydrocephalus and meningitis are the leading factors besides the constitutional infection which cause death.

Statistics.—Improved technic and rational diagnosis are improving the statistics of the operative treatment of brain abscess.

Oppenheim reports 60 cases of traumatic brain abscess operated, with 38 recoveries; 138 otitic abscesses, with 62 recoveries.

Oppenheim and Cassirer report 206 cases of otitic temporal abscess and 76 of otitic cerebellar abscess, of which 148 (70 per cent) and 35 (45 per cent) respectively were saved.

Macewen's statistics are most encouraging for he has had 18 recoveries in 19 cases of brain abscess.

Dench reports a successful issue in over 50 per cent of cases (100—with 52 recoveries). In his own practice he operated 18 cases with 6 recoveries.

Additional Considerations.—Extradural pus deposit offers an encouraging prognosis if operated early.

Otitic leptomeningitis (diffuse) is a fatal complication in most cases.

Otitic sinus thrombosis (purulent) if unoperated is always fatal. Recoveries may be expected in over 65 per cent of cases radically treated.

Lumbar puncture offers no data which influence prognosis. Diagnosis is strengthened in doubtful cases by the withdrawal and examination of the fluid.

Jacobsohn's concluding sentence in his consideration of the prognosis is worth quoting: "The prognosis of untreated abscess of the brain is very discouraging; spontaneous recovery is within the domain of the possibilities but in practice it cannot be considered. Without timely surgical interference the patient dies either in coma, at times in convulsions, or in other cases with sudden exacerbation of brain symptoms. In some cases death follows rupture with symptoms of fulminating meningitis."

The *duration* of brain abscess has been considered with the separate etiologic factors and the complications. As a rule the duration varies and in the more chronic cases, from whatever primary source developed, there may be a history which covers months or even several years of indefinite

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symptoms, at times only slight headache or recurring severe headaches. There are cases which finally terminate fatally after months during which there have been exacerbations of symptoms, at times severe, with improvement during several weeks or even longer periods. In some of these exacerbations there are rigors followed by severe headache and sweats.

Rupture into a lateral ventricle may lead to sudden death while meningitis, which frequently develops as the end sequel of abscess, may cause death in from three to seventeen days.

In chronic cases there may be after long latency a considerable period of pressure symptoms, edema of the brain, hydrocephalus with final rupture in the ventricle, or death after a few days of meningitis.

Cases of self cure, encapsulation or calcifications, are of such rare occurrence as to merit no consideration in offering a forecast.

Nature makes a supreme effort to control brain abscess or limit its spread by the formation of a connective tissue enclosure in chronic—at times acute—cases; this usually fails, for the abscess may extend in spite of its improvised wall. This protective process, however, is responsible for the latency of many cases which finally, as the result of fresh infection, trauma or other causes, either rupture, extend, or lead to leptomeningitis.

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8. *Aneurism*

See Tumors of the Brain and Aneurism

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III. Tumor of the Brain

General Considerations.—The insidious growth of brain tumors, the unfortunate localization of the majority, the frequent long periods of focal symptoms including Jacksonian convulsions, without marked advance, the erratic clinical behavior and the innumerable anomalies of a neoplasm in an organ which is not particularly tolerant to attack, all tend, with innumerable other factors to be presented in this chapter, to make the prognosis bad.

The leading varieties of brain tumor are:

(1) Tubercle
(2) Sarcoma
(3) Glioma
(4) Carcinoma
(5) Entozoa (Cysticercus hydatid)
(6) Syphiloma (Gummata)
(7) Abscess (Suppurative encephalitis)
(8) Aneurism.

Besides the tumors mentioned I have elsewhere in this work called attention to the occasional involvement of the brain with actinomycosis, and would call attention to the occasional development of *psammoma, cholesteatoma, angioma, adenoma, dermoid cyst* and other cysts following *hemorrhage* and *traumatism.*

In 6,150 cases of internal disease I diagnosticated brain tumor 13 times (excluding gummata), or .002 per cent of all internal diseases. In 9,626 cases of nervous diseases there were 165 brain tumors (Jacobsohn).

Bruns reports that of 4,300 patients who consulted him with disease of the nervous system, he found 80 in whom the diagnosis of brain tumor was justified (about 2 per cent).

Tumors of the cord are not so frequent as are brain tumors. Metastases to the cord are more frequent than to the brain. The percentage of men with brain tumor is 62.5 against 37.5 among women. Bruns' statistics of autopsied cases show the proportion to have been 23 males and 8 females in 31 cases.

Gowers' statistics run almost parallel with Bruns'. He found in 650 cases of brain tumor 440 men and 210 women. Starr based his conclusions on an analysis of 600 brain tumors and presents the following tables:

Age.—Most brain tumors develop in persons between the ages of 15 and 30 years. The second decade in frequency is between 30 and 40. More than one-half of Bruns' cases were between 20 and 40 years of age. Brain tumor in old age is exceedingly rare. Experienced clinicians and specialists in this field report the rarity of brain tumor after the sixtieth year. Bruns says he has seen but one case. Brain tumor in early life is

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TABLE I (THE FIRST COLUMN ARE CHILDREN'S TUMORS; THE SECOND ADULTS' TUMORS)

Situation	Tuberculous		Sarcomatous		Gliomatous		Glio-sarcomatous		Cystic		Carcinomatous		Gummatous		Other Varieties		Total
I. Cortex Cerebri	13	9	1	46	6	19	..	8	..	..	1	19	..	13	..	12	21–127
II. Centrum Ovale	6	2	5	7	1	11	1	4	15	..	1	3	1	..	5	4	35–51
III. Cerebral Axis:																	
1. Basal Ganglia and Lateral Ventricles	14	3	5	8	3	9	..	..	1	1	1	2	..	1	3	5	27–34
2. Corpora quadrigemina and crura cerebri	16	1	3	2	1	2	..	5	..	..	..	1	..	..	1	7	21–14
3. Pons	19	11	5	1	10	..	2	1	1	..	..	2	..	3	1	..	38–17
4. Medulla	2	..	..	..	..	1	..	..	1	..	2	..	..	..	1	..	6– 2
5. Base	..	3	1	3	..	2	1	1	1	..	1	..	..	..	4	1	8– 9
6. Fourth Ventricle	1	..	1	1	1	..	..	..	..	..	1	2	..	..	1	1	5– 4
IV. Cerebellum	47	8	10	13	15	8	1	6	9	..	3	..	..	..	11	10	96–41
V. Multiple Tumors	34	4	3	5	..	2	..	..	2	1	..	2	1	3	3	1	43–57
	152	41	34	86	37	54	5	25	30	2	10	31	2	20	30	41	300–356

The study of 1,277 cases reported by the authors included in Starr's Table II demonstrates the fact that 9 per cent of all brain tumors are operable.

TABLE II. PERCENTAGE OF BRAIN TUMORS REMOVABLE

Author	No. of Cases	Operable	Reference
Mills and Lloyd	100	10	Pepper's System, 1886, Vol. V.
Hale White	100	10	Guy's Hospital Reports, 1888.
Starr	300	16	Med. News, Jan. 12, 1889 (children).
Knapp	40	2	Intracranial Growths, 1891.
Gray	53	4	Sajous' Annual, 1891.
Gray	49	6	" " 1891.
Seydel	100	3	Verhand, Deut. Gesell. f. Chir., 1892.
Dana	29	5	Trans. N. Y. Acad. Med., Jan., 1893.
Starr	300	21	Brain Surgery, 1893 (adults).
Byrom Bramwell	50	3	Edinburgh Med. Jour., June, 1894.
Oppenheim	23	1	Die Geschwülste des Gehirns, 1896.
Bruns	33	3	Encyclo. Jahresbericht, 1896.
Starr	100	20	Personal cases to 1903.
	1,277	104	

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relatively frequent. Gowers claims relative immunity during the first five months of life. Tubercle may develop early (after the sixth month). About one-third of all cases of brain tumor are found in children. Gowers' statistics included 18.5 per cent of his brain tumors in the first decade of life, 14 per cent in the second—figures which tally very closely with those of Bruns and most other English, German, and American neurologists.

Social status does not seem to influence the development of brain tumor, except the tubercle which is more frequent among the poorer classes.

Metastases to the brain are less frequent than to the spinal cord. Carcinoma is oftener of metastatic origin than is sarcoma.

Traumatism plays only a small part in the etiology of brain tumor. While this factor is relatively infrequent, there are cases in which there is strong evidence in favor of the possibility of tumor development following injury. In such cases the tumor may follow closely upon the trauma, or a considerable period may lapse before symptoms develop. It must be remembered in considering the relations of traumatism to brain tumor that not infrequently it is found on careful inquiry that some suspicious and suggestive symptoms antedated the injury and that *the symptoms of tumor, glioma particularly, follow traumatism because of the rupture of vessels in the growth, the structure of which is enormously vascular.* This accident in an existing growth at once leads to unmistakable symptoms and prompt diagnosis.

I have seen cases in which the growth was so far advanced as to suggest *it,* as the cause of the fall which produced the injury. *The medico-legal aspect of this subject is exceedingly important and demands close consideration.*

Another important fact to be considered with the effect of injury is the enormous *tolerance of the brain.* In many cases of sarcoma, at times carcinoma of the brain, varying periods in different cases may lapse without symptoms in the presence of growths which are however promptly developed after shock, hemorrhage, or laceration of brain tissue.

Bruns denies the possibility of degenerative change into true malignancy in a hemorrhagic focus or in contused brain tissue, as advocated by Starr and Oppenheim.

There are cases in which following trauma, the tumor has developed directly in or close to the injured tissue. Oppenheim reports cases in which following a period of epilepsy, tumor developed (See also Hitzig, Thomas, Bartlett, Keen, and Annandale).

Aneurismal dilatation following injury is not likely to develop in a normal artery, but in vessels which are previously degenerated.

Heredity is not a factor of importance in brain tumor. Tooth contends that it is practically a negligible factor.

The *location of the tumor* materially influences the symptoms produced,

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as do the rapidity of its growth and the extent of infiltration. Tumors which originate in the meninges may, during a long period, produce compression without giving rise to symptoms; on the other hand, meningeal tumors (sarcoma) may cause symptoms early, severe headache, and one or more of the leading symptoms of brain tumor with early ocular and cardio-respiratory symptoms, depending entirely upon the part of the brain compressed. Tumors with multiple symptoms usually grow rapidly, and promptly undermine resistance.

Tumors which cause motor, sensory, and mental symptoms at the same time are as a rule, rapidly growing, often associated with meningitis; they are often unfavorable for surgical operation, and run a comparatively rapid course.

The leading *symptoms* of brain tumor are *either focal* or *general.*

Focal Symptoms

The focal symptoms depend, as do focal symptoms in all brain lesions, upon the location of the growth.

Increase of focal symptoms is proof of increasing infiltration, or increase in the size of the growth, or both.

Compression may give rise to but few or no symptoms; it may during a varying period cause symptoms due to increased cortical irritation, or as the compression persists it may lead to destructive changes and final paralysis.

The focal symptoms are unilateral as a rule; they include spasm, monoplegia, hemiplegia, paresthesias, hemianopsia, aphasia and apraxia, often paralyses of one or more cranial nerves (Church and Peterson, Starr, Bruns, Dana).

Hemiplegia which increases gradually, in which thrombosis and arteriosclerosis (endarteritis obliterans) can be excluded, is likely to be due to brain tumor and when present long before the radical operation in operable cases, is not encouraging.

Paralysis of two or more cranial nerves with or without hemiplegia, particularly when the nuclei or fully formed nerves are distant from each other, in most cases influences prognosis unfavorably.

The more complex the focal symptoms the greater is the danger in the individual case and the less likely is surgery to save the patient.

Focal symptoms dependent upon compression of the motor area, the radiating fibers, the superficial structures or other accessible parts of the brain in which the tumor is not infiltrating, offer a far better outlook than do those cases in which disseminated deposits are early recognized.

Mental disturbance, including hallucinations, with brain tumor and focal symptoms, with optic neuritis and paralysis, either limited or extensive, offers only the gloomiest prognosis wherever the growth is located.

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General Symptoms

The leading general symptoms are

(a) Headache
(b) Vertigo
(c) Vomiting
(d) Psychic disturbances
(e) Slow and irregular pulse
(f) Fever
(g) Spasms and convulsions
(h) Optic neuritis or optic atrophy
(i) Emaciation
(j) Weakness
(k) Constipation
(l) Venous obstruction.

(a) **Headache.**—Headache is the leading symptom of brain tumor wherever localized or whatever its build. The symptom is persistent, and is not easily controlled except in the specific deposits.

Nocturnal exacerbation of headache with symptoms suggestive of *luetic disease* offers a favorable prognosis. The symptom is promptly controlled in most specific cases.

The effect of *lumbar puncture* on this symptom varies; some headaches are favorably influenced. In occasional cases lumbar puncture aggravates the headache, in spite of the lowering of intracranial pressure which usually results.

The persistence of headache in one location, with local tenderness, may in occasional cases serve to assist in the localization of the lesion. Under such conditions the growth is likely to be superficial and often favorably located. Occasional cases have been reported in which the headache has been so intense and severe as to lead to suicide.

Starr believes that the distensibility of the skull in children is the reason for the milder character of the headaches in early life than in adults.

Subcortical tumors without headache, not too deeply located, with sufficient symptoms to localize the growth offer a favorable prognosis if operated early.

(b) **Vertigo.**—Bruns found vertigo particularly prominent as a symptom of cerebellar and frontal growths. The clinical and prognostic significance of vertigo is important for it assists in localizing the lesion and it is, in some cases, an epileptic equivalent (Church and Peterson).

(c) **Vomiting.**—*Vomiting* often assists in early diagnosis. Persistent vomiting has in a number of my cases caused extreme weakness and death.

In non-tuberculous brain tumor, vomiting is less likely to be an early symptom than with either tuberculosis or syphilitic deposits.

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Vomiting which persists with the characteristic features of *"cerebral vomiting"* is an early symptom of tuberculous meningitis (tubercle) and (specific) gummata. In the tuberculous cases of early, or even late life it may yield in exceptional cases but it is likely to recur before the stage of paralysis which ends the life of these children.

In the syphilitic cases vomiting yields as the patient is brought under the influence of specific treatment.

Vertigo and vomiting are often present together, the latter following acute exacerbation of the former symptom. These cases are often of cerebellar origin.

Vomiting and headache may cease during limited periods at times. When vomiting recurs after temporary cessation, the headache is likely to recur with increased intensity. At times both symptoms are promptly associated with stupor or other evidences of profound cerebral involvement —such behavior may be the precursor of an early fatal termination.

(d) **Psychic Disturbances.**—*Fully developed mental symptoms* are usually evidence of advanced infiltration; they are associated with other symptoms indicative of early death. In some cases of sarcoma, carcinoma, and gummata, there may be early psychic disturbance which persists without marked advance of deterioration. When *convulsions* are associated with mental weakness, the growth as a rule may be expected to lead to early death. In some cases mental symptoms and severe headache may be materially relieved during periods of varying length, to return with marked increase of pain and mental hebetude. *Persistent apathy* is unfavorable. Tumors of the frontal lobes are likely to be associated with mental symptoms, and these appear early with such lesions.

(e) **Slow and Irregular Pulse.**—Marked *compression* is usually associated with characteristic slow pulse during the early days of the disease. When the pulse, formerly slow and full, suddenly becomes rapid and erratic, intermittent or arhythmic, it may be assumed that death is imminent.

Tumors of the medulla or its immediate neighborhood without marked general features may cause the slow pulse and respiratory symptoms (Cheyne-Stokes) which together are always ominous.

(f) **Fever.**—In some cases *slight elevation of temperature early* is suggestive of tuberculous meningitis. *Sudden hyperpyrexia* with brain tumor is always serious, and may be due to invasion of the medulla. As a rule it is an expression of deep involvement; it may be associated with suddenly arising *glycosuria, polyuria* and great exhaustion. Death in such cases is not long postponed. Slight rise of temperature during the evening hours is frequent during the terminal stage of brain tumor, and is associated with wasting and erratic heart action. With persistent fever, delirium, rapid erratic and intermittent heart action, brain tumor ends life in a large proportion of cases.

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Meningitis may develop in the course of brain tumor causing fever, at times *sudden hyperpyrexia.* The added evidences of meningeal involvement are easily interpreted, and with increasing coma death follows in from three to seventeen days. *If hyperpyrexia is an early symptom, the duration of the meningitis is short.*

(g) **Spasms and Convulsions.**—Spasms and convulsions may be due either to limited (focal) pressure or to disseminated disease of the brain. With the latter the convulsions are epileptiform in character, and generally with the former the spasms are an expression of a lesion in the motor area.

General epileptic seizures in advanced life, occasionally early in life, may prove ultimately to be symptomatic of brain tumor—a diagnosis which may be confirmed in a large proportion of cases by *ophthalmoscopic examination.* Sixty per cent of all brain tumor subjects have convulsions.

Unless the focal lesion which causes *jacksonian convulsions* is removed, general convulsive movements will finally follow, showing advance of infiltration—extension of the growth. Early convulsive movements are limited, and with focal lesions aid in localization. With *lesions in the motor area* these early spasms may persist during a variable period, yielding finally to paralysis of the part originally convulsed.

Epileptic seizures dependent upon the pressure of brain tumor rarely yield unless the growth is removed. The prognosis even with operative interference is not encouraging, though an occasional case recovers. Without surgical relief the prognosis of all epilepsies due to tumors, save the gummata, is absolutely bad (See Epilepsy).

Convulsive movements are of great value in the diagnosis of brain tumor and often allow the early localization of the growth. Persistence of convulsions or spasm after surgical operations is unfavorable, such cases are progressive and fatal.

Convulsions may recur at short intervals, or they may be truly epileptic with long periods of freedom. In some cases these recur many times during a single day or during a limited period, to recur after several months of freedom.

In most cases persistence of convulsions or recurrence at short intervals should be interpreted as indicating rapid growth of the neoplasm. Death in convulsions is comparatively frequent with brain tumor. The association of *hydrocephalus* secondary to tumor or hemorrhage may provoke convulsions, and prompt death.

(h) **Optic Neuritis and Optic Atrophy.**—*Choked Disk.*—Changes which are easily recognized by ophthalmoscopic examination in the optic disk are, according to Bruns, the most important of all the general symptoms of brain tumor. There are but few cases in which optic neuritis is not present at some time during the growth of the tumor. Oppenheim

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reports optic neuritis in most of his cases and holds that the presence of choked disk ("Stauungspapille") is proof of organic disease of the brain and, "last but not least," is almost certain evidence of brain tumor (90 per cent).

Optic neuritis is present in the early stages of brain tumor; optic neuritis is usually present and easily recognized by the aid of the ophthalmoscope within three to four months of the beginning of the growth. When the papilla or disk is prominent and dips into the fundus, it is spoken of as *"choked disk."* *Optic atrophy* is a condition which may develop early, or may be postponed until the late stage of brain tumor. With the appearance of atrophy, the swelling of the disk, edema of the optic nerve or "choked disk" begins to disappear, while the whiteness of the papilla (atrophy) becomes striking. Such progression is characteristic of advancing infiltration and growth.

These ocular changes are most likely to occur with tumors of the cerebellum and with growths which involve the visual paths at the base of the brain. Marked prominence of the papilla (choked disk) is always suggestive of cerebellar invasion. Tumors of the chiasm are also associated with changes in the optic disk.

Optic neuritis occurs with nine-tenths of all brain tumors. Optic neuritis is a frequent attendant of meningitis. *Meningitis is not unusual in the membranes of the brain surrounding the tumor.*

Choked disk is not an early symptom of brain tumor save in growths in which the cerebellum and visual paths are involved, therefore without evidence of cerebellar invasion the appearance of choked disk or optic atrophy with other evidences of brain tumor must suggest advanced infiltration and an early unfavorable termination. The larger the growth, the greater the compression, the more prominent is the papilla. There are exceptions to this rule. Usually the more intense neuritis is on the side of the tumor. Starr, as the result of his large experience, says of optic neuritis: "It is present in 80 per cent of the cases and should be looked for in every case which presents cerebral symptoms."

Stewart holds that in time optic neuritis in most cases progresses to optic atrophy with its accompanying blindness.

Optic neuritis may persist during considerable time without blindness.

Optic neuritis and headache may improve after decompression without the removal of the growth. In cerebellar and frontal tumors the progression and greater intensity of optic change tends to be on the same side as the tumor.

(i) **Emaciation.**—Extreme emaciation may promptly develop after only a short period of symptoms; this often follows in cases with uncontrollable vomiting, in metastatic carcinomata (multiple) with primary visceral growths. In some cases the rapid loss of flesh with increasing heart weakness is striking.

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Glycosuria with rapid emaciation has been noted in a number of cases, particularly with tumors of the medulla.

Multiple growths (usually carcinomata, gliomata, or sarcomata) are likely to cause rapid loss of flesh.

(j) **Weakness.**—Extreme muscular weakness with rapidly increasing focal and general symptoms, often persistent headache which can only be controlled by enormous doses of morphia, presents a complex which may persist during several weeks or months. These are among the most pitiful pictures met in the practice of medicine.

(k) **Constipation.**—Obstinate constipation is present, and an annoying symptom, in a large proportion of cases. Directly obstipation does not influence prognosis unfavorably.

(l) **Venous Obstruction.**—The pressure of a large tumor, or one so located as to impede the venous circulation, may cause a certain degree of hyperemia (local). Cases in which the venous stasis is sufficient to be prominent have also general and focal symptoms associated, which makes it easy to prognosticate. The outlook is bad.

Some general symptoms usually precede the focal and in most cases the course of the disease is insidious, though there are many exceptions to this rule. *Remission and exacerbation of general symptoms are frequent, and often lead one to doubt the original diagnosis, but finally continuous symptoms with optic atrophy or neuritis, progressive emaciation, and mental hebetude cause death.*

Prognostic Influence of the Nature of the Growth

(1) Tubercle.—Tubercle is the most frequent neoplasm which invades the brain. Its presence may be tolerated without subjective symptoms during long periods. I have considered brain tubercle fully in the chapter on tuberculosis (Tuberculous Meningitis) to which the reader is referred.

(2) Sarcoma.—Sarcoma of the brain is second in frequency of occurrence. The growth may originate in the membranes of the brain or in the brain tissue or cord. There is a difference of opinion as to the consistence of the majority of sarcomata; Starr believes they are hard, while others consider them soft. In considering the clinical course and complications of cerebral sarcomata because of the histologic build of these growths, the absence of blood vessels in most, sudden apoplectic conditions need not be feared. The sarcomata do not infiltrate, are often encapsulated, and when operable are easily enucleated.

Sarcomata grow rapidly, are usually single though they may be multiple. When metastatic, the prognosis is absolutely bad. We have seen multiple and symmetrical sarcomata invading both halves of the brain. When springing from the bony structures at the base of the brain and

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causing pressure, also involving the brain tissue (osteosarcoma), the course of the disease is short.

(3) Glioma.—In the majority of cases glioma of the brain is a single growth. It may be multiple. It is the characteristic growth of the brain and nervous system and is not as a rule a circumscribed growth—which fact argues against a favorable outlook—unless removed early. Its favorite seat is the cerebrum; its rich vascularity invites rupture, consecutive paralyses, and at times sudden death from hemorrhage. Glioma of the brain is usually primary. *Gliosarcoma* of the brain is rare.

Spiller and others believe that their clinical material justifies the conclusion that glioma may exist many years "without causing symptoms and may be of comparatively slow growth." My experience in several autopsied cases corroborates this conclusion.

Depending on its location, tumors other than glioma may during long periods cause no symptoms; they may grow so slowly as to remain unsuspected and suddenly present with a fully developed train of symptoms which promptly lead to death.

(4) Carcinomatous Deposits.—Carcinomatous deposits in the brain are almost always secondary, are usually of rapid growth inclined to show multiple deposit, and as all cancers wherever found, are infiltrating. Brain cancer rarely develops early in life—usually after middle life. Brain symptoms following breast or distant carcinomata should at once make the diagnostician suspicious of cancer.

(5) Entozoa.—Cysts due to parasites may remain without marked symptoms during indefinite periods; they may on the other hand cause all of the symptoms of brain tumor, and with increasing symptoms lead to death. In some cases echinococcus may cause symptoms during a limited period, then become encysted, and remain latent during many years (See also Parasitic Diseases of the Brain).

(6) Syphilomata or Gummata.—Syphilomata or gummata of the brain offer a good prognosis if treated early and rigorously.

I have fully considered the prognosis of syphiloma (gummata) in the chapter on brain syphilis. *Of all brain tumors the gumma or syphiloma offers the most favorable prognosis.*

In my experience the iodids have only benefited or influenced cases in which the tumor was of syphilitic origin. It may be positively assumed that malignant growths—non-syphilitic—are in no way influenced by iodin, mercury, or by any medical treatment. Starr believes that in some cases he has seen good results, more particularly symptomatic relief from the use of the iodids.

(7) Abscess.—Abscess of the brain (suppurative encephalitis) is separately considered (See *Suppurative Encephalitis*).

(8) Aneurism.—Aneurismal dilatation of the cerebral arteries is

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also separately considered (See Miliary Aneurism in connection with cerebral apoplexy and the full consideration of arteriosclerosis).

Additional Considerations

My cases have all been found after the forty-fifth year, in which there were fair-sized tumors (aneurism); in all there were symptoms which strongly suggested the nature of the growth; in all there were pressure symptoms which persisted, usually involving the cranial nerves—one or more.

In the majority of cases the localization of the growth is made possible by the focal symptoms. In considering the separate symptoms and their pathologic significance I have frequently referred to the influence of location on prognosis. It should always be the aim of the clinician to localize as nearly as possible the seat of the growth. Unfortunately only a small percentage of exact localizations will lead to successful radical treatment.

The literature which has accumulated during the past two decades on the results of the surgical treatment of brain tumors, proves that only from three to five per cent of brain tumors make satisfactory recoveries, and less than seven per cent are operable.

The so-called "pseudo tumors" of the brain in which recovery follows are not veritable neoplasms, but present symptoms which resemble those of brain tumor. These are cases of meningo-encephalitis according to Oppenheim, and are often tuberculous. Recovery is often slow. Remnants of symptoms may remain (Nonne).

There are occasional (exceedingly rare) cases in which the diagnosis of brain tumor has been made, in which there is improvement of symptoms and apparent recovery due in all probability to *degeneration of the tumor.* In most of these cases after a limited period, particularly in the malignant cases, the symptoms recur and there are evidences of multiple or spreading disease and increasing compression. *With rupture,* escape of cerebrospinal fluid through the nose in tumors with hydrocephalus, the symptoms may, during a short period, improve or be partially relieved; but soon progression must be expected and death follows.

Focal symptoms with spasmodic contractions (jacksonian) due to cortical irritation (tumor) may yield in the presence of such tumor, to be followed by fully developed motor paralysis. In such cases there is no further improvement, but with increasing evidences of brain compression and motor insufficiency, the general and ocular weakness as well as other focal symptoms increase until death follows.

Symptomatic improvement may occasionally follow *lumbar puncture,* but never cure.

Lumbar puncture is not without danger to life in cases of brain tumor.

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Decompression may also relieve the symptoms in an occasional case, but the growth unless removed is in no way modified.

Enormous assistance for localization, treatment and prognosis may follow stereoscopic *x-ray pictures.*

Periods of latency with the persistence of but few symptoms, have occasionally led to erroneous prognosis. Such cases may remain quiescent during limited periods to suddenly advance with increase of exhaustion, optic neuritis and other symptoms, depending on the location of the tumor. In some of these cases with the *development of blindness* or *psychic disturbance,* the patient may continue to live during several weeks or months. Such cases are likely to die suddenly, or with increasing coma and evidences of added basilar meningitis death follows. There are recorded cases in which tubercle nodules and sarcomata degenerated, calcified, and their growth was inhibited. The echinococcus may die, and with an enclosing membrane and calcification may never give rise to symptoms (See Parasitic Diseases of the Brain).

Positive symptoms of tumor may disappear during considerable periods in which *repeated epileptic convulsions* have been the leading symptom. *Epilepsy* may be the only symptom of brain tumor during unlimited periods before the continuous or positive symptoms of the growth. With tumor and epileptic seizures, the former may remain unsuspected and the diagnosis is made post mortem.

The duration of brain tumor varies in accordance with its histologic build, its location, and the rapidity of its growth.

Tooth's analysis of *500 positive cases without operation* in which glioma was the most frequent growth (49.2 per cent), showed that in these growths the survival was from six weeks to nine years, "but only one case had so long a period." The average period was ten and one-tenth months. Tumors in the frontal region survive longest, the temporosphenoidal region next, and "the corona radiata" last. Tooth found the shortest survival period in tumor of the midbrain—"pons-cerebellum, and base of the brain—in which it was twenty-four days—this was a glioma of the pons; and the longest was two years, also a tumor of the pons." "The average survival period was nine and one-tenth months; not much less than that for the forebrain."

Endothelioma, according to Tooth, offers a better prognosis than the growths above mentioned; when operable it is not likely to recur. The average survival period in Tooth's cases was four years and it is held by his reviewer (Spiller) that "this figure errs on the side of underestimation."

Tooth's cases of pituitary tumor averaged seven and one-half years.

Most authors and clinicians give three years as the average duration of brain tumor.

Tooth's résumé of *500 cases of brain tumor operated* at the National

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Hospital during a period of ten years proves that a high mortality follows all operations on the brain "even in the hands of the most experienced surgeons." Simple craniectomy has shown a high mortality. All are agreed that the success of all operations is largely influenced by the location attacked. The danger is generally regarded by surgeons as greater in the cerebellar region, least in the region of the midbrain. Cushing finds cerebellar tumors favorable for attack.

In considering the factors which influence the results in operable brain tumor, we face the danger of shock, sudden collapse, respiratory and circulatory failure, including hemorrhage. The sudden respiratory or circulatory embarrassment may follow within a few hours, or late paralysis may promptly end life without a moment's warning several weeks after operation.

Hyperpyrexia following operation is not unusual, and with the Kernig symptom and other evidences of meningitis may end life within a few hours. Hyperpyrexia and circulatory embarrassment may, without evidences of meningitis, promptly cause death. There have been cases in which the removal of a growth of doubtful, but supposedly innocent build has been promptly followed by the rapid growth of near and distant metastases of a malignant nature, with increase of general and focal symptoms and death. This occurrence is purely accidental and does not argue against the radical treatment of all growths which are operable.

Tumors of the *hypophysis cerebri* have been successfully attacked of late, and with a growing experience the results are increasingly successful. The brilliant work of Schloffer, v. Eiselberg, Krause, Hirsch, and Cushing lead to the hope of greater accomplishment in this field in the future.

The palliative operations (trepanning the skull, decompression) are justified in properly selected cases, for they occasionally bring the relief which, if it does no more, gives the unfortunate victim an easy euthanasia.

Cushing justifies operative interference because among other benefits he includes "a Sellar decompression"—"the partial removal of a tumor or struma for the relief of neighborhood symptoms."

The hope of attacking the forebrain as well as the midbrain for the removal of growths is strengthened by the results of Horsley, Krause, Cushing, and a score of other operators.

Lumbar Puncture.—Lumbar puncture in brain tumor is not without danger and should be undertaken with great caution. Increased pressure (300-600 mm. Hg.) is not unusual. The higher the pressure the more serious the condition of the patient. In some cases the fluid is yellow-tinged, and in advanced tumor fibrin coagulum is found. There is but little albumin while Phase I (Nonne), i. e., globulin, is absent.

Cellular increase is not great and in the majority of cases does not exist. With specific deposit (gummata) there is usually lymphocytic and albumin increase. *Meningeal hemorrhage* with tumor shows blood in the

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fluid; such cases are grave. Cholesteatoma (basilar) shows cholesterin crystals and "fat needles," without albumin and cellular increase (Plaut, Rehm, Schottmüller).

Brain puncture in the hands of the expert will finally lead to localization of growths, will make clear their histologic structure and will thus assist in the diagnosis and prognosis (See Rothmann).

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IV. Parasites of the Brain

Echinococcus is fully considered in the preceding chapter on tumor of the brain.

The *cysticercus cellulosae* is rarely found in the brain in the United States; on the Continent it is relatively frequent. The prophylactic treatment of infected meat (Tenia solium) is reducing the number of these cases. *Solitary cysts are the rule* (Stern).

With the *death of the cysticercus* the contents of the cyst may calcify, and if fortunately located, symptoms may end and the patient may live without material handicap. The life of the cysticercus may continue from three to twenty years.

Echinococcus of the brain is a rare disease; but 22 of 327 echinococcus subjects were found with brain deposit. Cysticercus and echinococcus may be accidentally discovered post mortem without a suspicion of their previous existence. It is surprising to note how, with deposit near vital brain centers, both may continue latent and life not be disturbed. In the majority of cases cerebral parasites do cause symptoms which include many of those considered in the chapter on brain tumor. Most prominent are headache, vertigo, and mental disturbance. In some cases *neurasthenia, hysteria, epilepsy* and *well-defined psychoses* have been prominent.

Griesinger has called attention to the frequency of convulsions with brain parasites.

With growth and pressure, the *cranial nerves,* one or more, may become involved. *Optic neuritis, choked disk and atrophy* are less frequent than with the ordinary forms of brain tumor. Mild neuritis occasionally develops.

Cases in which *glycosuria, circulatory and respiratory symptoms* develop prove a dangerous localization of the tumor, and death is not long postponed.

Paralysis is not an early symptom and is not likely to develop in the average case. Cysticercus of the brain is always serious. It is often latent, as already suggested, and may be cured by nature's process at any stage of its existence. Oppenheim reports the case of a male patient who was treated during many years for cortical epilepsy of cysticercus origin (he also had cutaneous cysts) in whom the convulsions finally ceased, and he remained cured.

Lumbar puncture is of great value in the diagnosis of cysticercus and echinococcus of the brain, and in some cases prognostic data may also be obtained (Plaut, Rehm, and Schottmüller).

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V. Cerebellar Disease

In connection with tumor of the brain the prognosis of cerebellar growths is considered, a favorite and probably the most frequent seat of neoplasms.

With the exception of cerebellar ataxia, cerebellar tumor and abscess, cerebellar paralysis of children, and the arteriosclerotic and other vascular changes which lead to cerebellar symptoms, the other lesions of the cerebellum are unimportant, rare, and usually associated with disseminated disease.

Ataxia once fully developed with cerebellar disease, remains a permanent symptom—it is the leading symptom of such a lesion. The faulty equilibriation, tendency to fall or sway to one side, is also permanent and characteristic. The ataxia is always on the same side as the focal change or deposit, and the swaying is also toward the same side. In man, as in other animals, compensation may occur so as to "permit of but little evidence of incoördination."

Naturally congenital defects of the cerebellum—*heredo-ataxie cerebelleuse* (Marie) remain uninfluenced by treatment.

With *senile cerebellar atrophy* there are symmetrical changes, particularly in both hemispheres and in the cerebello-olivary fibers. The process is progressive and a part of an apparent general decay.

Cerebellar staggering due to arteriosclerotic changes in the vertebral artery—its branches, the basilar or cerebral arterioles—is usually associated with far-reaching change in the arterial tree, and persists. Cerebral apoplexy, uremia or cardiac insufficiency are the usual causes of death in these cases.

Besides arterial degeneration with sclerosis of the cerebellum, *hemorrhage* and *thrombosis* are among the vascular lesions.

Hemorrhage, as Nothnagel suggested, *may be suspected if, without motor paralysis at the beginning of an attack, vomiting is a persistent symptom.* There may be a considerable focus in the center of one hemisphere without paralysis, but there are other persisting symptoms of cerebellar disease.

Hemorrhage into the middle portion of the vermiform process may

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lead to dyspnea, deviation of eyes to the left, tremor of the left half of the face, great unrest, and respiratory paralysis. The nearness of the pons is the cause of hemorrhage into it and the cerebellum at the same time, with an unfavorable ending as a rule. *Thrombotic lesions of the cerebellum* are small, and may cause no symptoms.

The fact that the reflexes—patellar tendon—may in the same case at different times be either exaggerated, diminished, or abolished, does not influence prognosis.

Cerebellar lesions, tumors particularly, are "especially liable to *optic neuritis early* and in severe degree, leading rapidly to loss of sight and consecutive atrophy" (Russell).

Nystagmus is one of the most constant symptoms of cerebellar disease, though it is not always present.

Hemiataxia and hemihypotonia are characteristic of cerebellar ataxia and simulate hemiplegia at times. These symptoms persist. Hypotonia is also persistent and uninfluenced in almost all cases; it is characteritic of cerebellar disease. Bastian first called attention to the fact that muscular tonus is derived from the cerebellum.

With Wernicke's *polioencephalitis hemorrhagica superior* (alcoholic) (see Encephalitis), cerebellar ataxia and other focal symptoms with delirium and ocular paralysis form a threatening symptom complex.

Lesions which begin in the middle cerebellar peduncle usually invade the pons as they extend. Disease of the middle peduncle may remain stationary and "lesions which simply exert pressure on it may cause no characteristic symptoms" (Herter).

The prognostic significance of cerebellar symptoms, functional and organic, have been separately considered in connection with the systemic and indiscriminate lesions—hence repetition in this chapter is unnecessary.

There are many functional and organic diseases (multiple sclerosis, hysteria, neurasthenia, etc.) in which cerebellar symptoms are prominent; the prognosis is always influenced by the nature of the primary condition as well as that of the complication.

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D. Functional and General Diseases of the Nervous System

"Everything which vividly affects the mind, everything which powerfully stimulates the imagination, favors the development of hysteria in persons predisposed thereto" (Charcot).

1. *Hysteria*

General Consideration

To gain an approximate idea of the true nature of the complex process included under the head of hysteria, we must recognize that the underlying conditions are psychical; that clinically, hysteria must be considered a *psychoneurosis;* that it is not due to an organic disease of the nervous system; that it is a disease in which the "normal course of the psychical processes" (Strümpell) is disturbed and that their "association with the purely corporal processes of innervation" are also deranged. There can be no doubt that the initial anomaly is always to be found within the "psychic domain."

Hysteria is a condition which in its various manifestations may simulate true organic disease. Indeed, it may mimic disease of any organ of the body, and so closely very often that it frequently becomes an exceedingly difficult problem to decide between this psychosis, with its close resemblance to pathological conditions but without organic change, and organic disease with the hysterical accompaniment in the ascendency. The mimicry of true organic disease by a psychoneurosis (hysteria) is by no means easily overcome but should be considered to be a grave disorder—in spite of the fact that it does not destroy life—for the reason that it is rarely completely cured and that there are but few hysterical subjects who fail, when conditions favor it, to develop an ungeared condition in which the normal relations of the mind to the body are disturbed. In other words, such subjects promptly become "hysterical." While long periods of immunity may be enjoyed by these subjects, it may be accepted as true in the overwhelming majority of cases that a confirmed hysteric, one who has *"the stigmata of Charcot"* will always remain subject to the disease. The symptoms, one or many, will appear even after years of immunity under stress, or will follow one or more of the many inviting factors in the subject. The latter, because of an innate weakness, an inability to will, in spite of the fact that to will is his strongest desire, again falls into a condition in which constantly *recurring autosuggestion* gains the mastery. I assume that the *"hysterical symptoms"* in all cases, when (as not infrequently happens) such symptoms accompany organic disease in one or more organs are without

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pathologic fundament; that hysteria *per se* does not destroy life; and further that *the psychic element in the causation of symptoms or their disappearance is always predominant.*

The hysterical subject is a psychopath; there is the persistence of a vivid and ever ready imagination. Such a mental state justifies the definition of Möbius, who holds that "hysteria is any disease which is produced by the imagination."

At the very outset of the study of the prognosis of hysteria, before considering its separate manifestations, it must be forcibly insisted that under stress, particularly under emotion or excitement, under conditions (psychic) which would pass without influencing the mental processes of the normal subject, the psychoneurotic is likely to be ungeared, and falls into a condition in which one or more symptoms gain the ascendency and dominate his being. A further factor of exceeding importance is found in the fact that *at the bottom of almost all true hysteria is the congenital, the inherited anomalous, predispositon of the nervous system.* It is this *psychopathic* and *neuropathic condition* which leads me to the conclusions to which I have referred in the preceding paragraphs that when hysteria is fully developed, the patient is likely to become hysterical on slight cause even after long periods of apparent health. This does not mean continuous symptoms of hysteria, but the prompt awakening of a mental condition with full imagination and a train of symptoms characterized by their evanescence and mutability.

Considering the *influence of etiology upon the control of symptoms,* it is clearly evident, inasmuch as psychic causes—*emotion, excitement, shock, physical injury, terror, fear, anger or agitation*—provoke attacks, that the regulation of the life of the patient proves enormously advantageous in controlling symptoms and improving his mental condition. Whenever the attention of the neurotic patient is centered upon one part of the body, he becomes hysterical; he is, because of his own continuous suggestion, unable to divorce himself from the organ which has taken possession of his brain, and he continues in this mental attitude until by a stronger suggestion or a transfer of attention to another or several other organs, he is partially released. *Mutability of symptoms, their evanescence and rapid displacement are characteristic.*

When the psychoneurotic subject after long periods of worry or sorrow is finally disappointed, and suffers a single blow, which appears irreparable and which to him is of paramount importance, he may promptly become hysterical, and his condition is associated with *many symptoms* or *one* which is exceedingly distressing—*to him* always of transcendent importance. Such patients are controlled with great difficulty and yield only after long periods of suggestion and treatment. The average human being is provided with a nervous system which can easily withstand repeated insult and disappointment. The hypersensitive, with neuropathic

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tendencies are less fortunate, and held by faulty mental processes, their imagination gains control to the exclusion of normal activity.

The diagnostician in offering his prognosis is not to be misled by the *sudden cessation of symptoms* which have been long persistent, for the period of immunity may only be short-lived. The leading symptoms of one attack may never return, but a multitude of complaints which hold the patient with equal firmness are likely to be substituted during unlimited periods in the less tractable subjects, or the period of freedom from symptoms may cover years during which the unhealthy and disturbed imagination continues dormant.

So far as offering a forecast of *the behavior of individual symptoms in well-established hysteria* is concerned, it may be said in the average case that single symptoms will in almost all cases yield during varying periods to suggestion or other rational treatment, that in spite of conditions which mimic the gravest organic diseases, release may be predicted.

Psychic disturbances or events will always be found closely related to hysterical exacerbations or the awakening of a dormant, previously unsuspected, psychoneurosis into activity. The localization and persistence of symptoms are also enormously influenced by psychic factors; thus a *hysterical paralysis* may limit itself to the part of the body which was but slightly bruised or injured in an accident, and the same is equally true of the hysterical joint. *Such symptoms are often continued by an auto-suggestion which in turn is nurtured and sustained by litigation or other factors which bear forcibly on the future material welfare and happiness of the patient.* That the element of suggestion is decidedly in the foreground even in honest cases there can be no doubt, as is demonstrated in the consideration of the traumatic neuroses (See separate chapter—Traumatic Neurosis).

In the general consideration of the prognosis of hysteria, all agree that cases which are without strong predisposition to diseases of the nervous system, without enslaving heredity, which are so balanced that they have a sufficient remnant of healthy autosuggestion, are less likely to become permanently phychoneurotic than are those with a less favorable history; and in these subjects the prognosis for complete cure is relatively good.

The *acquisition of the neuropathic predisposition* is possible, and is among the unfortunate incidents of life; it may lead to years of wretchedness with a train of symptoms similar to those present with the *inherited disposition.* In the cases in which neuropathic-hysterical tendencies have been fostered and sustained, really developed by faulty processes and environment in subjects without hereditary taint, the imagination may be so encouraged as to influence prognosis unfavorably. The persistence of innumerable symptoms literally "disjointed," unreasonable from the pathologic point of view, during long periods, is characteristic of such cases.

The old theory which traced all hysteria to the *sexual organs* in both

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the male and female, has long since been discarded by the erudite clinician. It is exceedingly dangerous to become one-sided in our reasoning in connection with the etiologic factors which lead to this psychoneurosis; if we do, our treatment must of necessity suffer and prognosis is robbed of its rational fundament. There is a safe middle course for the diagnostician to follow; this divorces us in our prognosis from false premises and gives us the breadth of vision so much needed. I fully appreciate the influence of psychic-sexual factors in many cases, but forcibly deny their paramount influence in all cases of hysteria. The consideration of the possibility of the sexual causes in the individual case should be thoroughly weighed but the greatest discrimination and keenest judgment are needed lest we awaken in the subject a train of thoughts by psychanalysis which in the end may prove of serious consequences.

Unquestionably in a proportion of well selected cases the hysterical manifestations have been overcome by the so-called "cathartic method" of Freud in which, by psychanalysis, there are laid bare to the observer and to the patient the unconsciously repressed group of ideas against which the patient has been struggling and against which the hysterical manifestation represents a defensive mechanism. Once these repulsive ideas are brought to light, discussed and reacted to with the natural and appropriate emotions instead of being repressed as too repellant for thought, the need for defensive reactions vanishes and the hysterical manifestations disappear, while at the same time the disturbed emotional content becomes normal.

In offering a prognosis from the study of the separate symptoms of hysteria, clinical experience establishes the fact that symptoms which arise acutely in one case and which may be of short duration in others are often exceedingly rebellious and chronic. *This absence of any rule so far as the behavior of symptoms is concerned is characteristic.*

The disappearance of symptoms (*paralysis, spasm, anesthesia, paresthesia, vomiting, ocular symptoms*) suddenly, after mental emotion, sudden shock or other deep psychic disturbance, is to be expected, and with added suggestion and healthy occupation of the mind the clinical picture may be favorably influenced—in some cases permanently changed for the better.

The possibility of the *latency of symptoms* should be considered before offering a positively favorable forecast in cases which have simulated the organic diseases.

The tendency to *long periods of latency* in hysteria not dependent upon exogenous causes, needs to be repeatedly impressed upon the clinician in the study of the individual case. The forecast will always demand the full appreciation of the possibility of relapse in cases which are burdened by an unfortunate heredity or in which the environment during early life was unfortunate and often stifling.

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Heilbronner has emphasized the fact that the prognosis is most favorable in hysteria which originates from exogenous causes, rather than those in which "the habitual departure from the normal psychic type" has been in the ascendency.

There is no organic disease which hysteria may not simulate, but there is no organic disease in which symptoms are so evanescent and contradictory as in hysteria. In the prognosis of all types of hysteria the *emotional element* becomes an important diagnostic and prognostic factor to which we must cling. In prognosis, the great danger of suggestion by the physician should be studiously avoided for in the examination hysterical symptoms are often unearthed which when recognized by the patient, at once lead to the stimulation of the imagination and the consequent increase of subjective symptoms. Strümpell is correct in his statement "that numerous hysterical stigmata develop only through the medical examination, inasmuch as the ideas of the patients are influenced by the examination."

The ascendency of the *emotional element* in the hysterical subject is likely to persist.

Fully developed hysterical psychoses may last only during a short period (few hours) or they may persist during discouragingly long periods (months). In the end, the psychoses are favorably influenced by treatment, but whenever stigmata of hysteria remain in such subjects, their mental instability is likely to lead to psychoses.

Loss of memory—amnesia—is not a cause for worry. These subjects recover and by properly directed hypnosis, the void may be filled.

Hypnosis (suggestion) has proved a valuable method of relieving many of the unusual psychic abnormalities of hysteria *"dual personality" ("second etat")—hysterical melancholia, postfebrile hysteria* including *delirium, puerperal hysteria and other postinfectious neuroses.*

Anesthesia and Sensory Disturbances

When insignificant causes lead to supposedly grave symptoms as *widespread and complete anesthesia,* the hysterical fundament of such symptoms is easily established, and the prognosis becomes correspondingly good.

Total analgesia with sensory anesthesia, amblyopia, contraction of the visual field, anosmia, and other symptoms, readily recognized as of functional, psychic origin, offer a good prognosis. They are often promptly influenced by rational treatment and a strong personality (suggestion).

Complete hemianesthesia should always be interpreted as hysterical, for as Moebius has said, *"there is no organic lesion of the nervous system of which complete hemianesthesia is a symptom."* The symptom is often evanescent and yields, but in chronic cases is displaced by other sensory or visceral disturbances.

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Hemianesthesia after sudden shock, injury, fright or other factors, all acting promptly, with prominence of the emotional element, offers a favorable prognosis, but the "predisposition" insures only uncertain periods of freedom, a ready return to a condition in which the suggestibility of the patient makes substitution of a variety of symptoms possible and control often difficult.

Anesthesia which is characteristic of hysteria in a large proportion of cases is rarely recognized by the patient. The areas are indiscriminately distributed; they bear no relation to the sensory nerve distribution. The influence of psychic factors is paramount. Anesthesia may yield suddenly to either suggestion or deep mental emotion, or shock may prove a factor of paramount importance in causing prompt relief.

The *sharp line of demarcation* of anesthesia or analgesia which is characteristic of hysteria is at once of diagnostic and prognostic value. *Hysterical hemianesthesia* reaches to the middle line—no further; *organic hemianesthesia* is associated with *motor paralysis,* the cause of which is *easily localized.* It *does not yield to suggestion.* is not *evanescent,* there is *complete absence of mutability of symptoms*—all of which make the *prognosis of the monosymptoms of hysteria favorable.*

Absolute or complete sensory disturbances of hysteria within the area involved are always more favorable because complete anesthesias are not characteristic of organic disease.

Pain

The pains of hysteria may simulate the sensory symptoms of severe organic disease. Pains are not always easily controlled. Once the hysterical subject has pains with symptoms which are interpreted during fright as of grave organic origin, the element of suggestion assists to continue the symptom. This is particularly true of such cases as simulate *angina pectoris; in women with palpitation; a heart which is overactive* and strikes the chest wall with undue force; in certain cases of *pleurodynia with cardiac neurosis;* and with the *globus or clavus* in which the sense of constriction, weight, pressure or fulness "chokes" the patient. Such patients live during varying periods in constant fear of approaching death, and it is only by repeated assurance and suggestion that they are finally relieved.

Patients who have recurring pains in the precordium, with hysterical tendencies, particularly women who have *Glenard's disease* (gastroptosis, gastrectasia, mobile kidney with or without cardiac neuroses) are among the most difficult of all hysterical patients to treat successfully, unless they are removed from depressing and unfavorable surroundings.

The *lumbar and sacral pains* besides intercostal neuralgias frequently, when of functional hysterical origin, yield to treatment only after long trial. Many of these cases are associated with visceral disease—functional

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and organic—or there is some *constitutional disturbance,* often anemia. Cases in which pains are a leading symptom, wherever located, require the closest possible investigation as too many are diagnosticated as of hysterical or functional origin which finally prove to be due to grave cardiovascular lesions or disease of the nervous system.

The presence of few or many *hysterogenous points* have no bearing on prognosis; they are present in severe as well as in mild cases.

Special Senses

Symptoms referable to the organs of special sense are not always appreciated by the patient; when they are, fear takes possession and there is profound depression.

Taste and Smell.—Perversions of taste and smell are not, as a rule, persistent symptoms. Abnormal taste is limited to portions of the tongue and mouth.

Hearing.—When hearing is involved it is exceptional to find complete hysterical deafness.

Chavanne has demonstrated that with hysterical deafness there is more or less anesthesia of the auditory canal, of the head and the face, on the same side as the deafness. *Anesthesia* of the *tympanic membrane* is not frequent. None of these conditions are permanent.

Ocular Anomalies.—The leading ocular anomalies are fully desscribed by Parmaud, Gilles de la Tourette and de Schweinitz in "The Eye and Nervous System" (Posey and Spiller), and to these the reader is referred (See References). The leading features are:

(a) Contraction of the visual field
(b) Faulty color perception
(c) Errors of accommodation
(d) Hysterical blindness (amaurosis)
(e) Hysterical amblyopia (incomplete anesthesia of the visual sense)
(f) Hysterical asthenopia
(g) Hysterical pupillary phenomena
(h) Hysterical paralyses of the eyelid
(i) Paralysis of the ocular muscles
(j) Hysterical contractures
(k) Palpebral and bulbar anomalies.

(a) **Contraction of the Visual Field.**—*The concentric contraction of the visual field is the most prominent ocular symptom of hysteria.* It represents, according to Parmaud, "an insensibility of a portion of the field to white light, and this insensibility develops from the circumference to the center in such a way that a graphic drawing of the contraction

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would be represented by an almost circular line." The contraction of the visual field in hysteria may persist during long periods. Different cases differ, but in most, it does not yield so long as the psychic element is prominent. There are cases in which the contraction may continue during years; in other cases a few weeks or months prove to be the limit. The *variations in the size of the field* are insignificant until full recovery takes place. With recovery from hysteria the field returns to its normal size.

(b) **Faulty Color Perception.**—In hysteria, besides contractions of the visual field for form and light perception there is concentric contraction of the color fields (dyschromatopsia, achromatopsia and hyperchromatopsia).

In hysteria the normal order is changed. The color fields in the normal subject may be tested with "saturated colors in good illumination" and "occur from the periphery to the center in the following order: blue, yellow, red, green, violet." In hysteria the red field frequently exceeds the blue and "the color lines coincide or cross one another, or it may exceed it and become the most peripheral of the color circles" (De Schweinitz).

The disappearance of the color fields is in the following order, violet, green, blue, yellow and finally red. With lifting of the hysterical condition the faulty color perception is likely to yield, though it not infrequently happens that both contraction of the visual field and faulty color perception may persist long after the emotional element has been controlled.

(c) **Errors of Accommodation.**—The hysterical subject may occasionally present errors of accommodation which, as a rule, make near vision faulty.

(d) **Hysterical Blindness**
(e) **Hysterical Amblyopia**
(f) **Hysterical Asthenopia.**

Naturally hysterical blindness is most alarming, but the assurance may be given that vision will return no matter what the form or accompanying hysterical complex, without a remnant of the former defect. The duration of some rare cases of *amaurotic blindness* cannot be determined; however, cases in which *blindness continues during unlimited periods are in all probability of organic origin and not hysterical* (Sachs, Mauthner, Schmidt-Rimpler).

Hysterical blindness may appear suddenly, and is often lifted with equal suddenness. Patients with *unilateral blindness* see with both eyes, as may be readily proved by means of the stereoscope when the picture appears just as it should when viewed with both, and not with one eye.

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In hysterical subjects partial blindness is more frequent than the total blindness (amaurosis).

(g) **Hysterical pupillary phenomena**
(h) **Hysterical paralyses of the eyelids**
(i) **Paralysis of the ocular muscles**
(j) **Contractures of ocular muscles**
(k) **Palpebral and bulbar anomalies.**

The foregoing anomalies (g to k inclusive) are occasionally met with other ocular symptoms (contraction of the visual field and faulty color perception). They may simulate organic disease, but the emotional element with the associated symptoms irregularly distributed and their mutability, as well as the absence of all data which admit of exact localization with other stigmata of hysteria, prove their functional-psychic-character and justify a good prognosis. The possibility of the existence of *paralysis of the eye muscles of hysterical origin* has been warmly denied by many good ophthalmologists and neurologists. Binswanger has never seen, in a large experience, "any isolated paralysis of an eye muscle, and believes with Parmaud and other writers that the so-called hysterical palsies should be explained by what is sometimes described as an associated ocular paralysis." "There is a paralysis of movement and not of the muscles supplied by a given nerve."

Paralysis

Hysterical paralyses may mimic oganic paralyses; but in this, success is never complete. The cautious diagnostician will easily, in the majority of cases be able to differentiate, though in occasional cases he may hesitate during a limited period.

Monoplegia, paraplegia, hemiplegia, or indiscriminately distributed paralysis may be expressions of hysteria.

The tendency, through psychic influence to keep one—a single—symptom prominently in the foreground, is often exemplified by the behavior of the *hysterical monoparalysis.* The hand, a foot, an arm or leg may alone remain motionless and analgesic or anesthetic during unlimited periods awaiting a profound impression, shock, mental emotion, successful suggestion of transfer of symptoms, or a sudden awakening which cannot be satisfactorily explained before the return of emotion and sensation.

The return of power is complete in paralyzed extremities without any of the atrophy or the reaction of degeneration which characterize organic paralysis. In exceptional cases atrophy (limited) may result from long continued disuse, but this is never extreme and promptly disappears after a short period of activity.

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Hysterical paralysis of the vocal cords (aphonia) is probably the most frequent form of the functional hysterical paralysis. It yields to suggestion as a rule, promptly, though in some cases only after long periods; it is likely to recur on slight cause.

Hysterical paralysis disappears so soon as the paralysis of the will is relieved. Sir James Paget in his essays eloquently gave the following example, which may stand for all forms of hysterical paralyses:

"A girl who has will enough in other things to rule the house has yet not will enough in regard to her limbs to walk a step with them, though they are as muscular as ever in her life. She says, as all such patients do, "I cannot"; it looks like "I will not"; but it is "I will not will."

Spasm

Hysterical spasms may simulate grave forms of explosive nervous disease—epilepsy, catalepsy, uremic convulsions, etc.

So-called *"hystero-epilepsy"* is not to be considered as true epilepsy. The features are so different as to make diagnosis easy in most cases, and prognosis relatively good.

Hysterical esophagismus (spasm) may be either acute or chronic. When acute, it is likely to be the single prominent symptom during an exacerbation and yields to treatment; when chronic, the spasm recurs at varying intervals. Months may lapse between seizures in cases which at times offer almost continuous symptoms during prolonged periods. Occasional cases may follow hearty laughter, may be associated with hiccough, and are often suddenly produced by trivial causes—usually emotional. One of my patients, a neurotic man with large responsibilities suddenly develops esophagismus while eating a hearty meal or while laughing during a play; sudden disagreeable news may have the same effect. The spasm may not last more than a few minutes, or may recur during several hours if he attempts to swallow. No treatment has prevented recurrence.

Contractures

Contractures of hysterical origin "attain their maximum at once"—a factor which is of the greatest importance in differential diagnosis and prognosis. *Organic contractures are gradually developed. Hysterical contractures are not found without other stigmata of hysteria.*

Contractures with anesthesia (*hemianesthesia* often) in which the sensory symptoms are evanescent and in which with fresh recurrence of the latter symptoms, usually opposite areas are selected, will under proper control and after varying periods, recover—usually without a remnant of change.

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Reflex Excitability

The exaggeration of reflex excitability in the hysterical subject is often of great value in strengthening the favorable prognosis in contractures, paralyses, and anesthesias, which at times seem intractable. It may happen that in the hysterical subject, particularly after injury, the contracture may precede paralysis or the latter may never develop. *Such cases usually yield to treatment or to the settlement of the claim in cases which are litigated.* In all of these cases sudden and complete recovery may be expected.

Charcot repeatedly demonstrated that "the constitutional revolution" ended the contracture of individual cases. He also used the magnet to "provoke a transfer of the contracture to the opposite side," and further successfully predicted that in a large number of these transfers "the contracture will exhaust itself."

Hysterical Joints

Both Sir Benjamin Brodie and Sir James Paget called attention to the *joint manifestations* of hysteria which at times are refractory during long periods. The great hyperesthesia of the joint is striking and out of all proportion to the objective signs. These joints yield to proper treatment though it has been held by many that long continued joint symptoms of hysterical origin may ultimately, if unrelieved, lead to grave organic changes which persist.

The hysterical joint recovers as a rule, without deformity. Paget cites Flowers' case of a man "whose skeleton is at Marburg, who was encased by his relatives for twenty years in a space in which he could only sit with his limbs doubled up and in which he could have had only very narrowly restrained movements of his joints; yet his limbs did not become deformed and his joints retained their normal textures."

"Innumerable cases of *hysterical joints after years of contraction recover fully and without deformity.*"

Hysterical outbreaks, convulsions, hystero-epilepsy, cataleptic states, ecstasy and innumerable anomalous mental states may during varying periods remain in the foreground with or without a multitude of other symptoms; at times during these periods in which the psychic disturbances are prominent, there may be a disappearance of most of the preceding leading features, or a single symptom may remain unchanged. The prognosis of the single symptom is absolutely unfavorable, the outbreaks are usually controlled under proper guidance but no assurance can be given that relapse may not occur. In patients with the *"hysterical temperament"* and hysterical outbreaks, the prognosis for permanent recovery is less favorable than in those who have become psychoneurotic as the result of injury or depressing factors. The improvement of the *social*

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status of such patients, better homes, cheerful surroundings, and healthy suggestion, repeatedly change the character of symptoms and assist materially in the restoration of the normal balance. However troublesome the psychoneurosis and however discouraging the mental status of the patient to the layman, permanent mental alienation need not be feared.

Cases in which grave mental disease exists with the hysterical temperament and stigmata are occasionally met, but the latter complication is accidental and is not responsible for the former. It not infrequently happens that with the late nervous manifestations of tertiary syphilis the symptoms have a tinge of hysteria. The latter complication does not influence the course of organic and usually fatal disease.

The spontaneously arising *hypnotic hysterical conditions* include *catalepsy, periods of lethargy, somnolence and somnambulism.* These states may arise suddenly after excitement, disappointment or long continued worry. The period during which the symptoms continue varies in different cases. In my last case a young, sensitive, and confiding girl was disappointed in love; without warning she became cataleptic and remained so during six weeks. Her rally was as sudden as the fall.

Cataleptic conditions are dissimilar. One or more extremities may escape. The recovery is, as a rule, full and perfect. There are no remnants of rigidity, and the tendency to relapse is finally fully overcome in most cases. There are cases in which the cataleptic state has persisted during many years. Lancercaux reports one case which continued twenty years. The majority of cataleptic periods are short—a few hours; rarely more than a day or two.

There is as a rule, complete *amnesia;* the events of the lost interval can be recalled by hypnotic suggestion.

The "grande hysterie" of Charcot is not often repeated in this country or in Germany. In France, at the Salpetriere, these larger attacks were unquestionably nurtured by repeated suggestion. The full attack includes severe epileptiform convulsions with loss of consciousness followed by contortions and the "grand movements," and finally the "attitudes passionelles" which are strikingly suggestive. In the production of the "grand attack" the element of suggestion which leads to the stimulation of the ideas is fully accented by the attack.

Loss of *muscular sense* (perte de la conscience musculaire of Duchenne) may complicate hysterical hemianesthesia which yields with other hysterical stigmata under favorable conditions, though relapse is frequent.

Astasia-abasia—unsteadiness in walking, with or without eyes open (astasia) or unsteadiness in walking without true or full incoördination may be present in hysteria, and demand differentiation and interpretation. The withdrawal of ocular guidance causes greater disturbance in hysterical unsteadiness than in organic disease, true ataxia. Astasia-abasia may exist without other symptoms of hysteria.

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Burr reports a case of hysterical astasia-abasia occurring in acute multiple neuritis in which the history justifies the conclusion that both the functional and organic diseases were of alcoholic origin. Astasia-abasia is unquestionably dependent upon an amnesia, and in the majority of cases yields after a longer or shorter period.

Akinesia Algera (Moebius).—I have elsewhere called attention to akinesia algera of Moebius in which, because of pain on the movement of a limb, or on swallowing, or after any other muscular effort, the patient ceases to help herself and sooner or later becomes bedridden with characteristic symptoms; these seem to deserve separate consideration because, contrary to uncomplicated hysteria, these patients may die (See Akinesia Algera). All of my cases have been women.

The *mimicry of cancer by hysteria,* particularly of the breast and tongue often requires repeated reassurance before the mental pang is allayed. Neuralgic pains in any part of the body known to the patient to be liable to cancer, may start the mimicry of the disease.

"It is strange to observe the tenacity with which some of the patients cling to the most dismal view of their cases. Though nothing wrong can be felt or seen, and though months or even (as I have known) years may pass without any disease appearing, yet will they believe themselves on the brink of misery with cancer of the tongue" (Paget).

Internal Organs

Perverted Appetite.—Perverted appetite, at times *complete anorexia,* during long periods characterizes some cases with or without other visceral symptoms. In occasional cases women who fear an increase of weight or because of a psychosis refuse to take food, are only released after repeated suggestion.

Hysterical Vomiting.—Hysterical vomiting may continue during considerable periods. There need be no fear of starvation, for the majority either hold their weight or the loss is insignificant. It always strengthens the diagnosis of hysteria, when with vomiting, often apparently uncontrollable, there is a strong emotional element; these patients as a rule, suddenly return to normal conditions.

Constipation.—Constipation is one of the most frequent attendants of hysteria and at times true *obstipation* appears threatening. When this is associated with tympanitis, the patients, usually women beyond twenty-five, are filled with fears; they often have "delirious hearts." Such cases even with extreme meteorism are relieved, but recurrence of symptoms is the rule.

Diarrhea.—Diarrhea of hysterical origin does not debilitate as do the ordinary enteritides, but when *membranous colitis* is almost continuously present, the psychic depression resulting is unfavorable and in rare cases

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these patients are bedridden—often during long periods—and are only raised by the overpowering influence of the attendants, change of scene, and oft-repeated reassurance.

Membranous Colitis.—Membranous colitis is often one of the most persistent of all hysterical conditions. When the patient has been brought to understand that the passage of intestinal casts or large mucous masses is never serious, that it may be present and continue during years without influencing the general health, that it yields in the end, the horizon is cleared and there is almost at once a decided change in the attitude of the patient.

Fecal Vomiting.—Fecal vomiting and long periods of intestinal inertia are among the rarer stimulations of organic disease. I number among my cases, one which recovered after thirty days of obstipation. The diagnosis in this case was made easy by the previous history of a train of symptoms, including hysterical paralysis with the prominence of the emotional element.

Menstrual Anomalies.—Menstrual anomalies in young hysterical subjects may materially influence the symptoms in individual cases; most of these irrgularities yield after a limited period, often with improvement or disappearance of the hysterical accompaniment.

Hysterical Cough.—Hysterical cough is a frequent symptom in young children, girls usually; it may recur during adult life on slight cause; it is almost always of the same character—paroxysmal and barking—and is in most cases promptly influenced by change of climate or scene, if not by suggestion.

Vasomotor and Secretory Disturbances.—Vasomotor disturbances as well as secretory disturbances are separately considered (Nervous Dyspepsia, also Diseases of the Sympathetic System). It often requires the clearest judgment after the full consideration of the history of the individual case to decide whether there is simulation, imaginary disease, or an organic lesion.

Hysterical Fever.—Hysterical fever offers a good prognosis. That psychoneurotics of the severer types develop fever—hyperpyrexia—on slight cause is positively established. Here too, the diagnostician must remain alert. Hysterical fever cannot be diagnosticated until all possible sources of the hyperpyrexia have been eliminated. Hysterical fever does not usually lead to great loss of weight; the period of convalescence is short.

Trophoneuroses.—All of the trophoneuroses of hysterical origin are without significance. They are easily recognized as a part of rapidly following evanescent symptom complexes without a single feature to justify the suspicion of organic change.

Sexual Anomalies.—Among the most intractable conditions are the *sexual anomalies originating in the imagination of the patient.* These are more frequent in the male than in the female. In the male the psy-

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chic element which leads to sexual weakness, impotence and the perversions of the sexual function is often in the foreground and is relieved only by the greatest tact and most powerful suggestion of the attendant, with the coöperation of those who have a moral right to be interested. The prognosis of this condition is often improved by reading to the obsessed patient extracts from the classic lecture of Sir James Paget on Sexual Hypochondriasis (see Reference end of chapter). In women there are sexual perversions of hysterical origin which make these patients exceedingly wretched at times. These too are relieved by proper treatment and honest suggestion unless there is associated organic disease of the brain.

Hysterical Tachycardias and Bradycardias.—The hysterical tachycardias and bradycardias are among the symptoms which promptly ungear the hysterical subject. Most of these patients, especially those who are normally neurasthenic, often become panic stricken with either of these anomalies; often the globus is added. The accompanying *faintness* adds an element of alarm, and the *fear of death* takes possession of the patient. Recovery with recurrence on slight cause, until the general and the mental conditions have been returned to their normal balance, is the rule.

Hysterical Torticollis.—I have seen a number of cases of hysterical torticollis in girls at or near puberty. Some of these were associated with convulsive attacks of the large type; others seemed to bear a close relation to genito-urinary anomalies. None of these were permanent. One continued to recur during a number of years, to disappear after the removal of a large *dermoid-ovarian cyst.*

Additional Considerations

This chapter might be extended to include the mimicry by hysteria of almost all organic disease. Such treatment of the subject is unnecessary, and would prove to be a work of supererogation. In the consideration of hysteria as well as in the differentiation of organic diseases such possibilities cannot be ignored, neither can the fact be overlooked which I have previously accented that *organic disease may be materially influenced by that psychoneurotic element (hysteria) which is present in both men and women*—oftener in the latter. It will often prove exceedingly difficult in such cases to separate the symptoms of the organic process from those of functional origin, and to give to each its prognostic value. *With the more serious diseases of the nervous system (multiple sclerosis, multiple neuritis, tabes dorsalis, myelitis, arteriosclerotic processes involving the brain and cord, cerebrospinal lues), the addition of a troublesome psychoneurosis may not shorten the life of the victim but it has a powerful influence in making him exceedingly wretched.*

In private and dispensary practice whether hysteria is associated with organic disease or not, it is evident that among certain people (Jewish par-

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ticularly) the element of psychoneurosis is so powerful as frequently to thwart the efforts of the therapeutist.

To lift these unfortunates above the level which makes them wretched through the exercise of an imagination which is encouraged by heredity and environment requires changed social conditions, hygienic homes, right living and release from economic slavery in which the toiler is without the means necessary to provide adequately for himself or those dependent upon him.

In a large experience I have but rarely found *organic disease following hysteria*; it is so rare as to justify the conclusion that when it does occur it is purely accidental. I fail to recall a single death positively traceable to uncomplicated hysteria. *When in a hysterical subject death is charged to the psychoneurosis, thorough search will reveal the presence of some organic disease.*

Resistance may be reduced by the so-called *hysterical vomiting.* In the overwhelming number of these cases organic disease of the stomach, toxemia or other pathologic fundament is found responsible if death occurs.

The favorable *influence of change* from the location in which the symptoms originated or from the surroundings in which the accident occurred which awakened the dormant hysteria to activity, is often of inestimable value, for it not infrequently—particularly in young subjects—dissipates all symptoms and materially changes the prognosis for the better.

It cannot be too often nor too forcibly impressed upon the clinician that hysteria is a disease which is not easily overcome. Thorough investigation of those who have shown symptoms during a prolonged period will rarely fail to disclose one or more of the stigmata, always present during the remission. *Children offer a better prognosis than do adults;* after thirty-eight or forty the prognosis for full restoration is not encouraging.

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2. *Traumatic Neurosis*

(*Traumatic Hysteria, Railroad Spine, Concussion of the Spine*—Erichsen)

The diagnosis of traumatic neurosis or traumatic hysteria is occasionally justified, but it must be remembered that following trauma there are so many factors which encourage *autosuggestion,* and in the designing *simulation,* it requires the greatest circumspection to separate the spurious from the honest cases. There are in most cases no symptoms which suggest the presence of an organic lesion; indeed *the psychoneurotic element is constantly present. Suggestibility is a leading feature and the differentiation of hysteria and traumatic neurosis is in many cases impossible.*

The complex of symptoms does not as a rule, develop immediately after the injury, but days, weeks, or months may lapse before a train of continuous symptoms follow which may, to the inexperienced, simulate grave disease of the nervous system or disease of other organs of the body. It is surprising to note how quickly after symptoms develop, the mimicry of organic disease is complete; how within a few hours there is often paralysis of the hysterical type; how within an unreasonably short period these patients become self-centered; how the *ego* is at once placed prominently in the foreground; and how in cases which lead to litigation, the worry associated with the approaching trial makes thought of almost all else appear insignificant to the litigant.

In honest cases of traumatic neurosis it will be found that there is an *inherent weakness of the will, a neuropathic predisposition which is often inherited.*

Evidences of this ungeared condition of the will with symptoms of hysteria—traumatic neurosis—following injury, may at times in the subjects of true organic disease be present, and may add an element of contradictory symptoms which in the end offer the same prognosis as do those exactly parallel, without the presence of preceding organic disease.

Litigation begets "litigation symptoms" (Page) *as will be demonstrated in this chapter, and the fate of these symptoms depends very largely, in the majority of cases, upon the termination of the litigation.*

Repeated autosuggestion during periods of uncertainty exerts an enormous influence in continuing the symptoms. The verdict in a large proportion of cases is expected to bring the means for restoration and the

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healthy suggestion is only commenced, when because of the successful issue the goal has been reached, or with continued inactivity and paralysis of the will in unsuccessful cases, poverty and ruin must be faced. Thus the end of litigation, favorable or unfavorable to the plaintiff, becomes at once the most important factor in the prognosis of litigated cases of traumatic neurosis.

It is unsafe for the clinician to follow Erichsen whose description of "Spinal Concussion" includes all kinds of lesions following railroad injuries without external evidences of the accident at any time. For years this work proved to be the fountain from which innumerable lawsuits sprung; it was, so far as the doleful prognosis which it gave, the ready support of the plaintiff against the railroads and other corporate bodies. Page came on the scene in 1881 and his work on "Injuries of the Spine and Spinal Cord" has done more to overthrow the authority of Erichsen than any other work. The essay of Page was based upon thorough clinical study and scientific observation.

In considering the prognosis of traumatic neurosis following accident, it must be assumed by the unbiased observer and diagnostician that the spinal cord is the best protected of all of the organs of the body; that in cases of traumatic hysteria (neurosis) there is no evidence or positive objective sign of a true organic lesion of the cord or its encasement; that *injuries which are of sufficient force or extent to give rise to symptoms of organic change are severe, immediate, and are likely to prove continuous or fatal.*

Fracture of the spine, crushing injuries, stab wounds of the cord, and dislocations at once lead to the symptoms which permit of a correct interpretation of the extent of injury to the nervous structures (cord, meninges and peripheral nerves).

The symptoms following what Jonathan Hutchinson called a "shake of the cranial contents without structural lesions of importance" are purely neurotic-psychic symptoms; as such they should be considered and discussed, and on such a foundation prognosis should be based. Whether we accept the classification of Oppenheim (1889) and consider the term "traumatic neurosis" justified or whether we accept the *dictum of Charcot* of the *purely functional nature* of all symptoms in cases without evident organic change, and further agree that it is impossible to differentiate these cases from true neurasthenia and hysteria, is of little moment in framing the prognosis, for *with a settled mind, the element of fear, suggestion, and all other depressing factors eliminated, the prognosis is correspondingly better and full recovery is the rule.* I exclude from consideration of this subject all injuries of a surgical character in which there are evident lesions and in which there has been organic change, the result of such injury, in which cases such changes take place as to make exact localization easy and positive. In the majority of such cases the

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symptoms are immediate, and the prognosis depends upon the extent of the injury—always graver than in uncomplicated traumatic neurosis.

With organic injury, as the result of fright, sudden shock, or from other causes in neurotic patients, true psychoneurosis (traumatic neurosis) may develop and prove stubborn and persistent.

The *surgical conditions* must always be separately considered; each offers its own prognosis.

There are cases of traumatic neurosis—usually with *hysteria in the ascendency*—in which there is no thought of litigation, in which serious and paralyzing conditions may continue during surprisingly long periods.

The *depression* and *changed mental attitude* of the patient who suffers from traumatic neurosis may lead to a train of symptoms already referred to as "litigation symptoms," which in many cases are honest and in all cases offer a good prognosis for restoration of function.

The *persistent melancholia* which characterizes some cases of traumatic neurosis, as Oppenheim has demonstrated, does in a few instances, differentiate these forms of the disease from true hysteria. The prognosis of this condition is good, though improvement may be slow and full recovery is often long postponed.

Traumatic neurosis may at times include *"psychic attacks"* resembling *epilepsy* (Westphal) or as Nonne has demonstrated, attacks of *hystero-epilepsy,* with or without direct injury to the head.

Localized muscular spasm and convulsive tic, without loss of consciousness, are not infrequently present in fully developed cases. These conditions usually yield with the other symptoms.

Arhythmia, "nervous and irritable heart action," is not unusual. The heart may behave just as it does with non-traumatic hysteria, and the prognosis is almost always good. I have seen no case in which *traumatic neurosis per se lead to organic disease of the heart or arteries.*

Goldscheider, Oppenheim, and Leers believe that *dilatation and hypertrophy of the heart and arteriosclerosis* may proceed from traumatic neurosis.

When *Graves disease* or other organic nervous or *cardiovascular changes* follow traumatic neurosis, it is likely that these diseases would have developed without the trauma. It cannot be denied however, that accident and shock are factors in lighting Graves disease to activity.

Vasomotor symptoms, including *cyanosis, abnormal blushing, dermographia* are usually evanescent and if they recur, as they often do, are finally fully controlled.

The manifestations of traumatic neurosis may be as numerous as are those of non-traumatic hysteria, and the prognosis of the individual symptoms must be considered in connection with the individual case.

It is positive that the neuroses with *monosymptoms offer a less favorable prognosis for prompt cure than do those with multiple symptoms.*

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Psychic disturbances which are not promptly relieved are likely to persist during unlimited periods. Cases in which organic changes have followed after *electric shock*, in which later the element of traumatic hysteria is developed, offer an unfavorable prognosis because the changes in nerve tissue are not, as a rule, overcome, and the wretchedness of the patient is sufficient to continue suggestion which does not permit of escape from the added traumatic neurosis (Jellinek).

The severity of the trauma does not stand in direct relation to the severity of the nervous manifestations. Insignificant injury may lead to obstinate neurosis.

Occasionally traumatic neurosis leads to *suicide*.

The most chronic and previously intractable case may recover after years of symptoms; often the improvement is sudden and unexpected.

Heredity and alcoholism always influence prognosis unfavorably.

What is the influence of traumatism on the development of general paralysis? Certainly traumatism does not make the syphilitic subject immune, but as Meyer has said "it is apt to add to the chances of precipitating the cerebral reaction;—traumatism will hardly be able to bring about the paralytic brain changes without previous syphilis." I believe the association to be purely accidental.

I have never known death to follow uncomplicated traumatic neurosis. Previous arterial and renal disease affects the prognosis unfavorably. It is impossible to give any opinion of value which will determine the duration of any case of traumatic neurosis. The factors of greatest importance, besides those already mentioned are: age, the nature of the psychosis, the previous history and the time of the existence of symptoms, the nature of the treatment received, as well as the environment of the patient and his circumstances.

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3. *Neurasthenia*

(Nervous Prostration, Nervous Exhaustion, Beard's Disease, The American Disease, Nervenschwäche)

General Statements.—Neurasthenia is rarely a primary disease; it is almost always *secondary* and furnishes a complex of symptoms which is encouraged by *lowered dynamic energy, lack of normal recuperative power, inherent weakness, an unstable mental state,* and *persistent autosuggestion.*

I would define neurasthenia therefore as an anomalous condition without substantial disease discoverable in nerve structures, in which there are abundant evidences of weakened nerve force, tendency to exhaustion, lack of reserve, increased irritability with, in the majority of cases, mimicry of organic disease, with a radiation of symptoms to parts distant from the supposed disorder, depending largely upon the self-suggestibility of the patient.

The unusual mental character of the neurasthenic and the predominant emotional element are characteristic, and powerfully influence prognosis. *Such mental characteristics* "good or bad, higher or lower than the average, something outstanding or sunken" *brand the neurasthenic; they are often inherited, and because of this fact the prognosis for complete release is relatively bad.* The "ego" is always in the ascendency; self-effacement is impossible; the mind is set upon some supposed grave organic disease; and continuous autosuggestion is practiced.

Neurasthenia has been spoken of as an "American disease." It is not a modern disorder, nor can it be considered a purely American disease. The symptoms of this complex were known to the ancients, and Hippocrates described diseased conditions resembling it hundreds of years ago. Beard and Bouchut made no revelations in medicine when they described this condition, for mention was made of kindred conditions by Sydenham, Robert Whytt, Raulin, and Pomme, while Hasse published cases of neurasthenia in 1855 taken from a German clientele exactly similar to those described by Beard.

Neurasthenics in whom there is no attending or provocative disease—primary neurasthenia—early in life show the "irritable weakness" which characterizes all neurasthenic states. Such individuals are born with *lowered resistance,* their *cerebrospinal system* and *cellular elements* lack the ability to rebound after even ordinary strain; throughout their entire lives, the neurasthenic complex is ready to come to the foreground on slight cause. The prognosis in such cases for full recovery is bad. Long *periods of freedom* from a multitude of symptoms may lead to the belief that the condition has been overcome; on slight cause, very often there is a return of neurasthenia, and the persistent suggestion continues to influ-

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ence the lives of these patients. The brain is often abnormally active but is easily fatigued and the patient soon learns his limitations.

Stewart makes the unmodified statement that "neurasthenia is not a primary disease," that it is always "exogenous" and the "result of something else." In those predisposed, usually between twenty and fifty years of age, the most frequent causes are mental or physical strain. Neurasthenia is more likely to develop in the active and productive than in the laggard, and in such subjects it proves to be a serious handicap because of its persistence, often during many months, and the tendency to recur on slight cause.

Cleghorn found in 6,000 cases that the complex was more frequent in men than in women and that two-thirds of his cases were between the twentieth and fortieth years of their lives. *Sedentary habits* in all cases aggravate the symptoms, and *idleness* invites the suggestion which leads to the neurasthenic state.

Causes.—*Idleness* in those predisposed to any neurosis is one of the leading causes of the neurasthenic state, and makes it impossible for the patient to regain the equilibrium necessary to make him normal. The unoccupied man has only himself to consider; he may suffer from a minor ailment or acute indisposition when his mind dwells upon it to the exclusion of all else; he sees in his symptoms only the gravest significance and this imaginary gravity takes possession of him. *Luxury, idleness, and the faults of modern civilization* are at work to rob the predisposed of their resistance; judicious occupation brings with the dissipation of the symptom complex, happiness, a sound mind, organs ready to fight disease, and banishes the emotional element which is often predominant. The neurasthenic without associated organic disease, who continues self-centered, who has one or more symptoms continuously before his mental vision, cannot recover without sufficient mental pabulum included in an honest suggestion and a healthful occupation.

Unquestionably the leading features to be considered in prognosis are the *influence of race and heredity.* This fact is forcibly impressed on the clinician in connection with his Jewish clientele, for the Jews are enormously neurasthenic; dispensary practice in all large cities furnishes the majority of cases. The predisposed are likely to become neurasthenic in *high altitudes.* Any condition which lowers vitality or adds any other inviting factor in subjects with "neuropathic inheritance" provokes anew the train of symptoms included in the complex, and unfavorably influences the prognosis; such patients do not die, but they are exceedingly wretched with one or more symptoms prominent and the associated and characteristic fear of impending death.

Insufficient early discipline, absence of self-control and failure to live the normal and average life, influence the resistance and recuperative power unfavorably.

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Faulty hygiene with improper education are potent factors which rob these patients of the power to lift themselves above the condition into which they usually fall on slight cause.

The influence of the occupations on neurasthenia is paramount. *Occupations* in which *worry* and *excitement* are almost continuous, in which the neurasthenic is unable to prevent the formation of toxins which result from fatigue, are injurious to the neuropathic subject, and unless changed, the prognosis for complete restoration remains bad. *Occupation* often improves the condition of these patients if it is agreeable and there are no associated worries or undue excitement. It is surprising to note how the confirmed neurasthenic often responds to suggestion and an occupation which keeps his brain active without fatigue, and how the heart under such conditions is kept light. *Work* in favorable surroundings which the patient enjoys, which is permissible unless the underlying pathogenic factors make it impossible, often leads to the dissipation of all or most symptoms.

Associated Conditions.—Neurasthenia may follow or be associated with *the infections,* particularly *influenza, typhoid, syphilis, tuberculosis, pneumonia,* and other *acute and chronic bacterial disease.* The prognosis in these cases depends largely on the patient's antecedents, the life which he leads and his ability to get the needed treatment, change from his unfavorable surroundings if indicated, and a variety of factors which for prognosis need to be faced in the individual case.

A surprisingly large number of *influenzas* are followed by neurasthenia. This is particularly true of such patients as return to their occupations before they have fully regained their strength and are of neuropathic habit. The brain worker, who has been reduced by grippal infection, of sedentary habits, whose occupation is associated with large responsibilities and many risks, recovers slowly unless he is given complete rest and the necessary relaxation. Most neurasthenias following grippal infection recover fully after long periods, though the graver psychoses not infrequently develop. Remissions and exacerbations are not unusual.

Gouty patients, the *diabetic* and the *alcoholic,* transmit to their offspring a *lowered resistance, limited endurance,* and the *predisposition* which lead to a *self-centered state* in which neurasthenia becomes predominant and is eliminated with the greatest difficulty.

In practice we find the most rebellious cases in the subjects of *cardiac neuroses* and *gastro-intestinal disturbances,—Glenard's process* particularly.

Traumatism and the resulting neurasthenic state has been separately considered (See Traumatic Neurosis).

In connection with the consideration of the prognosis of neurasthenia the fact may be once more accented that patients with inherent tendencies, or those who for some other reason are without normal resistance, are likely

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to develop the full train of neurasthenic symptoms after either slight or severe injuries. *The perfectly normal subject without neuropathic tendencies occasionally develops neurasthenia after strain or injury.* In such cases the prognosis is relatively better than in those who by habit are neurasthenic.

The most unfavorable cases are those in which the neuropathic tendency, with weakened resistance and abnormal nervous development, is imparted to the offspring of those whose habits and modes of life are in direct antagonism to all that is healthful and uplifting. It will be noted further that the prognosis is less favorable in those in whom baneful influences (heredity and environment) make it impossible to shake off minor ailments. The prognosis is far better in the "willful" than in the "willless."

Clinical Varieties.—The clinical varieties of neurasthenia derive their names from the organ or set of organs to which the leading symptom in the individual case is referred. With the neurasthenic condition pointing to any one of the organs most frequently the seat of symptoms (the brain, the spine, the stomach, the prostatic urethra, the genitalia, the eyes, the liver, the intestines, the heart, the uterus, the ovaries, etc.) modern methods of diagnosis in a large proportion unearth underlying anomalies which may be relieved by treatment, with relief often of the neurasthenic symptoms.

Cerebral neurasthenia, or as Beard characterized it, "cerebral exhaustion," may be a symptom of disturbed circulation—*cardiac asthenia—faulty blood states, faulty assimilation or metabolism* including the effects of *toxins, ptomains, acidemia, oxaluria, phosphaturia,* and a variety of other abnormal conditions which time and patient study of the individual case will detect and often relieve with consecutive relief of the cerebral asthenia.

Patients frequently present with symptoms referable to the spine (*spinal neurasthenia*) in whom the underlying cause proves to be *venereal excesses, changes in the generative organs* which are of themselves often insignificant; at times there are constitutional disturbances. *The sexual neurasthenic* is a difficult patient to influence. He has, as a rule, been misled by designing quacks or debasing literature which has magnified his symptoms, and has started an almost continuous self-suggestion which is depressing. At times these patients fall into a *melancholy or hypochondriacal condition* after a period of uncomplicated neurasthenia, from which they are raised but slowly. A strong personality with convincing suggestion often leads these patients from darkness to light.

Among the most intractable neurasthenics are those who, as the result of repeated suggestion have become *"sexual hypochondriacs."* Repeated *nocturnal emissions,* the slightest cloudiness of the urine, *imaginary impotence,* a slight *discharge of mucus, remorse after a period of masturbation,*

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premature emission during coitus, all impress the neurasthenic and interfere with recovery, until by thorough diagnosis and honest suggestion the patient is enlightened and released.

In cases of sexual neurasthenia without suspicion of congenital inferiority, especially the "anxiety neurosis" of Freud, a careful examination of the urogenital tract should be made for sources of reflex irritation. Often when the neurosis has been attributed to the psychic effect of improper sexual habits, to the sudden cessation of normal sexual life, to chronic masturbation, coitus interruptus, or premature ejaculation, it will be found that while these conditions are present, they are concerned only indirectly and that the nervous and psychic symptoms are directly conditioned by an actual irritation of some part of the genital tract; often this is to be found in a congested verumontanum and posterior urethra, in which region the genital reflex is believed to originate. If we assume that the constant stimulation of the sexual centers to which such a condition would give rise is equivalent to constant sexual excitement without adequate and normal discharge, it is easily understood why such widespread nervous and psychic symptoms should result. With the source of irritation discovered and proper local treatment applied, the prognosis for the neurasthenic symptoms is entirely good.

Sexual anomalies in women are often as rebellious as in men. The recurrence of sexual neurasthenia is often discouraging; most cases finally recover.

Factors Which Influence the Course of the Disease.—The *urinary anomalies* which have been charged with provoking and continuing neurasthenia, in a preceding paragraph, including *phosphaturia, oxaluria, hyperacidity, quantitative increase or reduction of secretion* demand close study in individual cases. In most cases, usually men, the control of the appetite, temperance in the use of wines and liquors, the discontinuance of the use of tobacco (often badly borne), the return to rational living, the leading of a normal sexual life with local treatment as needed, will prove sufficient to overcome most neurasthenias dependent upon the so-called diatheses.

In occasional cases it has been found that the effect of operation for varicocele has had a beneficial effect. Such patients often make permanent recoveries if the operation is followed by right living and a healthy suggestion, while before the operation they were self-centered and the gravity of their trouble was continually before their mental vision.

I have already mentioned the frequent occurrence of neurasthenic symptoms with *cardiac neuroses.* Grave organic heart disease in the face of approaching death is rarely associated with marked neurasthenia. It is with the cardiac neuroses that fear takes possession of the patient. The most chronic types of neurasthenia (marked tendency to recurrence) in practice have been associated with cardiac neuroses. *Periods of latency*

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are followed by long periods of persisting symptoms just so soon as the *arhythmia* or other evidences of faulty heart action appear. Complete cure is not infrequent.

The muscular weakness promptly following any well directed effort, true *myasthenia* often, in which sustained effort is impossible, may lead to chronic invalidism in which the patient finally becomes bedridden and cannot be induced to make the necessary effort to arise. Some of these patients spend years in bed and never recover. The "personal equation" of the attendant becomes an enormous factor in the prognosis of these cases; it is this class of neurasthenics which is often favorably influenced by some one of the many unscientific cults. Recovery in these cases may be sudden, unexpected, and complete.

The *increased tendon reflexes* in neurasthenia are without prognostic significance; as in hysteria the reflexes are usually increased.

Fear and imagination are among the most frequent accompaniments of the neurasthenic state; it not infrequently happens that the neurasthenic manifestations may suddenly disappear when *psychic disturbances* (*psychasthenia*) continue during unlimited periods. Under such conditions *fear* or *phobias* may take possession of the patient. These symptoms may disappear after a limited (short) period; at times the cases remain unchanged during a number of months, or symptoms recur on slight cause.

The *phobias* of true neurasthenia are as a rule easily controlled, and are often entirely dissipated by reassurance and the correct interpretation of symptoms for the patient by one in whom he has full confidence.

Arteriosclerosis, according to Watson and others, is not an important factor, *per se*, in the causation of psychoses, more particularly involution, and when present in the neurasthenic does not *per se* exert a marked influence on the prognosis of the symptom complex.

Psychasthenic states invite insanity. Neurasthenics who have fallen into the habit of sleeping badly, in whom the primary or predisposing cause has been removed, will after a few nights of induced sleep learn to sleep and promptly improve.

"Neurasthenic habits" can be overcome and many symptoms may in consequence be relieved, but to succeed requires the reassurance which accompanies repeated healthy suggestion and enormous attention to detail, as well as tact.

Paralysis and abolished patella tendon reflex are not present in neurasthenia without organic disease—neither are there anesthetic areas.

In considering the prognostic significance of *ocular* and *aural symptoms* it should be remembered that they are preëminently those of fatigue rather than of the mimicry of organic disease. With the removal of the cause, the blurring of the eyes and the sensitive eyeballs and aural disturbances are relieved.

The *sensory symptoms* of neurasthenia are numerous and exceedingly

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troublesome. They include besides *headache,* which is one of the most constant attendants, a variety of sensations referred to the head, "splitting," occipital pain and tenderness, "throbbing," "beating," "hammering." All of these sensations are not truly painful, but as Church and Peterson say "rather some variety of discomfort difficult to describe." Other sensory symptoms include peculiarly located and persisting *backache, tender spine* (superficial), *sensations of heat and cold, numbness of the extremities, prickling, stinging sensations, paresthesias, persistent "tired feeling,"* and a variety of abnormal sensations which may be referred to the abdominal, the genito-urinary, the pelvic or the thoracic organs without the earmarks of organic disease.

Gastro-intestinal anomalies are unquestionably present with neurasthenia in a large proportion of cases. The association of *Glenard's disease* with *neurasthenia* is surprisingly frequent and obstinately chronic. Such patients are often handicapped and made more neurasthenic by *faulty elimination, toxic conditions* and the association of *heart neurosis.*

Constipation is a frequent attendant. The relief of the constipation and support to the abdominal viscera which should also include the support of the mobile or prolapsed kidney and the general treatment of the neurasthenic habit (change of scene, wholesome suggestion, and repeated reassurance) lead to long periods of freedom from symptoms, and in some cases complete cure.

The *"brain fag"* or *"mental fatigue"* which is associated with muscular fatigue, yields with the removal of the underlying cause. In some patients who find that return to their original work causes *headache* and *prompt fatigue,* change to *out-of-door occupation* which includes exercise short of fatigue causes prompt improvement, often relief of symptoms during indefinite periods.

There is a class of neurasthenics in whom the *ocular symptoms* are in the ascendency, fatigue of accommodation promptly follows the use of the eyes while there is also more or less *retinal hypersensitiveness.* These patients are materially improved—often cured—by change of scene, rest during a limited period, and the correction of existing errors by the ophthalmologist.

The ability of the therapeutist to control the general condition of the neurasthenic depends very largely upon the associated disturbance, the organs from which the reflexes radiate.

Emaciation with Glenard's process, the nervous dyspepsia of Leube, with *sexual neurasthenia,* is by no means serious nor threatening and may promptly yield under favorable conditions—often more promptly than do cases in which the general nutrition has remained unchanged.

Faulty nutrition of the body—malassimilation of food—is one of the chief factors in the production of the neurasthenic state; this fact fully

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appreciated by the clinician in his treatment, will lead to marked improvement, often full recovery.

To discuss fully the prognosis of neurasthenia and all of its manifestations would take us into almost every field of medicine. Each of the many specialists to whom these cases find their way has a chapter to add which demonstrates to him the paramount importance in prognosis of his own limited field. All, however, if evenly balanced appreciate the importance of recognizing the underlying *inherent weakness* with which we must reckon in the prognosis of the complex.

Success means coöperation of physician and patient. The latter must be willing to strive "after self-effacement"; he must have ideals which lift him from the depths to which he has fallen; he must return to an occupation which will bring strength; he must learn to bear his suffering with equanimity. If the clinician has the hearty coöperation of the patient and his full confidence, the prognosis of neurasthenia is not bad; it is often cured, though as I have frequently held in this chapter, recurrence must be expected. Much depends upon the ability of the patient to take advantage of change of surroundings and he must have freedom from care and the many anxieties of life. A single but persistent *mental pang,* may be sufficient to continue the complex indefinitely in the predisposed subject.

The course of neurasthenia is chronic. The asthenia, growing muscular enfeeblement, and tendency to do less and less from day to day, impress the patient until the "irritable weakness" is fully established.

The prognosis is best in those cases in which the attendant gains the *coöperation of the patient;* in those who are able to take advantage of complete *change of scene;* in those who are not *burdened with an unfavorable heredity; who have been piloted without the formation of an enslaving drug habit.*

The younger patients, those who develop the disease before the twenty-fifth year, may improve after short periods of symptoms, but relapse is to be expected. In older patients, those beyond middle life, the prognosis naturally depends upon the underlying cause of the complex. With persistent functional or organic disease in such subjects, the neurasthenic accompaniment is not easily overcome, though it often happens that with increasing evidences of organic disease (bodily infirmities) the symptoms of neurasthenia may give way to those of the graver disease.

The recognition of neurasthenia as a symptom complex—secondary as a rule—will prompt the clinician to search for and remove the cause, thus improving the prognosis in the individual case. The regulation of the lives of those who lack normal recuperative power and the education of those with inherent weakness and an unstable mental state ever ready to practice autosuggestion, will go far toward reducing the number of neuropaths.

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4. *Paralysis agitans*

(*Shaking Palsy, Parkinson's Disease* (1817)

General Statements.—Paralysis agitans is a disease of unknown pathology characterized by *trembling of the extremities,* one or more in the early stages, later of the trunk and entire body, with *marked tendency to muscular rigidity* and *ultimate slowing of all movements,* increasing weakness, and premature ageing of the patient. The trembling may, in occasional cases be limited to one-half of the body during long periods, extending finally to the unaffected side; or the disease may remain limited and follow a chronic course without progression (See Parathyroid Therapy below).

While paralysis agitans is a disease of advanced life, when it attacks patients during middle life there are evidences in the early turning of the hair, the facies, the movements, and in the cardiovascular tree, of *premature decay.*

Arteriosclerosis is not a cause of paralysis agitans, but its presence with other evidences of premature changes have been strikingly characteristic in our material and demand attention for diagnosis; prognosis is materially and unfavorably influenced by the presence of rapidly advancing arterial change.

Juvenile forms of paralysis agitans (Stier) are occasionally found with characteristic symptoms including tremor, muscular rigidity and unsteadiness on standing. *In the advanced stages* locomotion is almost impossible. Such symptoms may begin early and persist during mature life. In all of these cases the clinician, before he offers a final prognosis,

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must fully satisfy himself that the symptoms are not of hysterical origin. Mendel asserts with positiveness that all paralysis agitans which begins before the fortieth year should always arouse a strong suspicion of hysteria. For prognosis and differentiation of the juvenile type the absence of sensory symptoms and the persistence of muscular tension during sleep, argue against hysteria and modify prognosis unfavorably. The gradual increase of symptoms without the history of traumatism or litigation, also argues in favor of paralysis agitans and against hysteria.

Willige found in studying 47 cases of so-called "juvenile paralysis agitans"—all of which commenced before the thirtieth year—only 12 in which the diagnosis was positively justified.

Frequency.—The frequency of paralysis agitans in practice is demonstrated by the statistics of Curschmann who found 5 cases among 300 inmates of an institution which corresponds with our "poor houses" or "county hospitals." Berger's report of Parkinson's material included 37 cases among 6,000 diseases of the nervous system; Mendel's material offers 50 cases in 25,000 cases of diseases of the nervous system (.2 per cent); my material included 28 cases among 6,300 internal diseases carefully cross-indexed (.04 per cent). It may be concluded that relatively the disease is rare. The disease is more frequent in England, Germany, and France, than in Southern Europe; strikingly frequent among the Irish. McCarthy makes the statement that "it does not seem at all rare in America."

Factors Which Influence Prognosis.—Erb found men more subject to the disease than women (5:2). Hart's material corroborates Erb's conclusions; his proportion of males and females in 219 cases was 7:4. *Poverty, exposure, mental strain and traumatism are inviting factors.* In one-fifth of the cases at the Berlin Clinic there was a history of traumatism.

In Gowers' material the average age was 52 years for the onset of symptoms. My material includes cases which commenced after the seventieth year and progressed slowly; the majority of these "senile cases" died of intercurrent disease; their general health seemed unaffected by the neurosis. When they lived over ten years after the onset of symptoms, the progression was slow, as a rule.

The influence of *heredity* on the prognosis of paralysis agitans is insignificant. In the material at my command I have only rarely found the disease among other members of the family. The positive statistics given by Lundborg of familial types of the disease, also its association with the familial types of myoclonus are not generally accepted by those, including Erb and Wollenberg, who have had ample opportunity to study a large material; and the latter warn against the consideration of heredity for diagnosis or prognosis.

From a cautious study of the *pathogenesis and pathology of paralysis*

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agitans, we are unable to offer reliable data from the included material. In our own country, the painstaking reports which Dana, Gordinier, and others have presented to the profession, including atrophy, pigmentation, vacuolation, and other degenerative changes in the cells of the anterior horns, etc. (Dana), and the perivascular sclerosis (Gordinier and Redlich), have not been confirmed.

The myogenic hypothesis including changes in the muscles offers nothing positive, though it has been strongly supported by Camp in an able article (See References).

Parathyroid Therapy.—The theory which has recently interested the profession and which seemed to some, because of improvement after the administration of the parathyroid substance (Alquier, Lundborg, Mobius, Berkeley) to favorably influence prognosis, is based upon the hypothesis that paralysis agitans is a symptom complex due to *disturbance of internal secretion.* Alquier's report of the histologic changes found post mortem of a sclerotic hypo or hypoplastic nature have not been confirmed, neither have others paralleled the favorable results of Berkeley following the administration of the parathyroid. The *hypoparathyroidism* of these reporters and the favorable prognosis based upon their conclusions have been strongly controverted by the claims of Roussy and Clunet who found *epithelial hyperplasia of the parathyroids causing hyperparathyroidism.*

The encouragement for prognosis which would seem to follow if we accepted without question the enthusiastic reports of those who claim success or improvement from parathyroid treatment is not justified by the observations of Greenwald, who at the chemical laboratory of the Montefiore Home in New York has conducted a series of experiments which prove that the acid-soluble phosphates in the blood serum of patients with paralysis agitans is not greater than in normal individuals, which would be the case if there was true parathyroid insufficiency. Tests with his material "do not support the view that parathyroid insufficiency plays a role in the etiology of paralysis agitans." We must, therefore, reluctantly refuse to base a favorable prognosis on parathyroid therapy.

Course of the Disease.—Tremor once established, is not likely to disappear. There may be periods of remission, or under excitement, exacerbation, but in true Parkinson's disease, while years may pass without marked increase of the tremor, it continues a prominent symptom with the variations characteristic of individual cases and *increasing rigidity* as the disease progresses. *Paralysis of the trembling arm and leg* (hemiplegia) as a rule causes cessation of the involuntary movement.

Muscular rigidity is unrelieved by any known treatment; it is more important for diagnosis than is the tremor, and is the most prominent and diagnostic symptom of the disease.

Paralysis agitans may exist and progress without tremor ("sine agitatione"), entirely uninfluenced by treatment. The rigidity is persistent;

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slowness of movement fully established is also continuously present with marked resistance to passive movement.

The characteristic *stooping posture, the hold of the hand and arm, the facial expression* (lack of expression) and *"trotting gait"* continue so long as the patient is about. The *tendon reflexes* offer no data of importance for prognosis. As the disease progresses muscular contraction is tardy and there is, according to Borgherieni, reduced irritability of the muscles and nerves to the electric current.

During the many years of persisting symptoms the *sphincters* are not involved; when they are, late in the disease, due to complications, the end is not usually long postponed.

In my material the *mental condition* of the patient has not been influenced by the disease; when it has been, the change was due either to *arteriosclerotic complication, senile dementia,* or *acute and added infection.* The *urine* offers no data in the average case.

It may be safely concluded that while the disease, *per se,* does not cause death, it is incurable by any known methods of treatment. There is a strong tendency in some cases to latency, indeed in some, the development is so slow as to remain almost entirely unnoticed. There are cases in which there is perceptible progression during periods varying in length in different cases, with stationary periods of short or long duration, often following, of considerable length. I have recently seen the chronic case of a woman about sixty-five years of age who, despite the presence of lively tremor of both upper extremities and a characteristic "trot," was able to dance the modern dances without unusual fatigue, and this in a public ballroom. The tremor in both arms persisted while dancing, the head was well controlled and the legs seemed to give no trouble.

Complications.—*Fractures and other trauma* in advanced cases as a rule aggravate existing symptoms.

Unless patients die within the first twenty to twenty-five years with progressive symptoms and acute or chronic complications in the majority of cases the rigidity advances to such an extent as finally to make locomotion impossible, and they become bedridden. This however has been an exceptional experience in my material. The chronic cases when bedridden, are likely to develop bedsores, cystitis, ascending genito-urinary infection with evidences of general sepsis; often pneumonia, marasmus, or other intercurrent disease.

Complications referable to the nervous system which affect prognosis unfavorably are hemiplegia, the association of chorea and epilepsy in cases with hereditary taint, perforating ulcer of the hand or leg, locomotor ataxia, hysteria, and joint changes resembling arthritis deformans (Spiller)—in one of my cases meningitis.

Patients with paralysis agitans are not immune to the infectious, constitutional, or local disease, and they often develop these. As a rule, it

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has been my experience that the resistance to added disease is materially reduced in the presence of shaking palsy.

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5. Chorea

(Sydenham's Chorea, Chorea Minor, St. Vitus' Dance, Infectious Chorea)

"Everything connected with this disease is extraordinary; its name is ridiculous, its symptoms singular, its course unusual, its cause unknown, and its treatment problematic."

While some of the problems associated with chorea are being cleared, the statement quoted from Bonteille (Preface of his "Traite de la Choree," 1810) is in the main true today. We are fast establishing facts however, which prove that chorea is a *hyperkinetic disease, which in the majority of cases is either directly associated with infection or follows it.*

Chorea is a curable disease of the central nervous system, usually of childhood, characterized by motor disorders, irregular, involuntary mus-

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cular contractions—all purposeless—which may continue during rest but are likely to cease during sleep, and are increased by excitement and emotion. Children and adults with chorea in most cases show psychic disturbances, more or less, in accordance with the natural tendencies (neuropathic) of the individual or the severity of the disease. The disease should be considered a *neurosis,* and the presence of *endocarditis and arthritis* at some time suspected.

History.—Chorea minor as a disease *per se* dates from Sydenham who in 1686 and 1693 fully described it and divorced it from the conglomerate mass of conditions with which it was associated during the middle ages (hysteria, mania, epilepsy, etc.).

Naturally the prognosis of chorea depends upon its cause and the associated pathologic lesions.

Conditions Which Influence Chorea.—*Sex.*—The disease is found to be more frequent in the female than in the male. Osler in his classic monograph reports 554 cases of which 161 were males and 390 (70 per cent) females. Gowers' ratio of females to males is 3 to 1. Wollenberg's statistics in 3,595 cases show 30 per cent men, 70 per cent women.

Age.—Heubner holds that chorea minor is not a disease of the suckling babe; but 3.6 per cent cases are found between the first and fifth year; from 6 to 15 years, 75 per cent (the larger number between 9 and 11 years); between 16 and 20 years, 13.5 per cent, while chorea after the twenty-fifth or thirtieth year, particularly among men, must lead to the suspicion of organic disease—Huntington's hereditary chorea, tic, or other central lesions (Wollenberg). The *senile form* of chorea is usually one-sided.

Moisture and exposure exert an unfavorable influence on those predisposed, and bear the same relation to chorea as they do to mono or polyarthritis. The influence of cold is further established by the greater frequency (50.5 per cent) of all cases during the four winter months (Czerno-Schwarz u. Lunz).

Unfavorable hygienic conditions, faulty homes, and *overcrowding* are factors which unfavorably influence the course of all forms of infectious chorea. *Heredity* does not materially influence the prognosis of acute chorea, depending as the disease does on infection. Wollenberg in 539 cases found but 2 per cent in whom there was a direct hereditary influence. It should be assumed however that in children who show the *hereditary neuropathic tendency or habit,* chorea is more easily developed than in those with normal resistance.

The Negro and American Indian seem to show a decided immunity to the disease. Of 175 cases at the Johns Hopkins Hospital 5 were in the negro race (Osler).

Psychic disturbances aggravate symptoms when present, and are unquestionably inviting factors in the presence of infection. Thus *fright*

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and *worry* in children often during examinations or tests in school, *overstudy, masturbation,* and unusual and *prolonged application* to one line of work may be included. In almost all of these cases, careful inquiry will establish a source of primary infection which may have been latent or active. The majority of *"imitation choreas"* are of hysterical origin and yield to rest and removal from school or from the unfavorable atmosphere of infectious chorea.

Associated Diseases.—**Tonsillar Disease and Chorea.**—*Nasal infection* associated with or without preceding nasal abnormalities, as well as *tonsillar infection, may not only lead to chorea but may be the underlying factors in continuing the symptoms during long periods. The removal of the primary focus* exerts a favorable influence on the course of the disease. In my experience I have found on careful investigation that the majority of tonsillitides which have been associated with chorea developed joint symptoms, and in most of these there was, as shown by physical signs (in the presence of murmurs), positive evidence of endocarditis.

Arthritis and Chorea.—The association of infectious arthritis with chorea is undeniable; the former is distinctly a cause of the latter, and unquestionably the disease is continued and sustained by the same microorganic life and its toxins which may be considered to have been the pathogenic factors of the primary disease.

Pathologists are fast subscribing to the dictum of Poynton and Pain which has received confirmation from the researches of Rosenow, which declares acute polyarthritis (rheumatic fever, inflammatory rheumatism) to be due to the streptococcus rheumaticus or some modification of the ordinary streptococcus (Rosenow), and upon this conclusion we are entitled to base the prognosis of a large number of choreas. There is association with arthritis or rheumatism in between 25 or 30 per cent of choreas, according to reported cases. This percentage is too low, for the thorough investigation of my material proves the presence of some symptoms of rheumatism, often only mild and suggestive in the majority of cases—over 80 per cent. This is corroborated by the data given by Curschmann and others. I have rarely found malignant endocardial infection associated with rheumatism and chorea. I lost one case—a girl of 8 years of age with malignant endocarditis, unquestionably of the streptococcus viridans type, after a period of subacute polyarthritis followed by the chronic type of malignant endocarditis and chorea which persisted several months before death.

Additional Diseases.—Richards also reports two cases of chorea with streptococcus viridans infection. The prognosis of such cases is almost uniformly bad; most patients live during several months and finally die with evidences of *multiple hemorrhagic infarcts.*

The prognosis of chorea associated with *purpura rheumatica* is good,

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though recovery is often slow. *Chorea with polyarthritis and gonorrhea when associated with endocarditis* offers an unfavorable prognosis. Chorea following or associated with *grippal infection* runs an average course to recovery in almost all cases, psychic symptoms which are prominent in some yield but slowly; these cases may relapse at short intervals during varying periods.

While chorea may be associated with most infections of childhood—scarlet fever particularly—the acute infections as a rule, when developed at the height of the disease, are likely to check the movements or dissipate them entirely.

Chorea gravidarum

Pregnancy is a provoking cause of chorea; it is in all probability due to toxemia; is most frequently present during the first half of pregnancy and in subjects who during childhood or later, had the same disease. Chorea during pregnancy is as a rule severe, not easily controlled, and is likely to be associated with active psychic disturbances. Mild forms are the exception. The prognosis is grave for both the mother and child. Frank reports 182 cases with a mortality of 23.6 per cent, for the former, and 4.7 for the latter. Oui reports 10-12 per cent mortality among the children. The prognosis for the mother is materially improved with termination of pregnancy by artificial means.

Factors Which Influence Prognosis

Ocular Errors.—It not infrequently happens that persisting chorea is favorably influenced by the correction of existing *ocular errors.* The safe conclusion to reach after a full study of the literature of this subject, including the original articles of Stevens, C. S. Bull, and De Schweinitz seem to me to be included in the statement of the latter quoted by Osler, "that ordinary chorea and many of the forms of facial spasm, habit spasm, etc., are materially benefited by correcting refractive errors and anomalies of the ocular muscles, just as they are helped by a variety of other treatments, but I do not believe that there is any proof to show that eye strain of itself is responsible for their origin, with perhaps the single exception of the so-called habit spasm affecting the orbicularis and immediate facial area. Certainly many of these will disappear promptly after the refractive error is corrected without any treatment whatsoever, and they will not disappear if you do not relieve the eye-strain. In a constitution predisposed to chorea I presume eye-strain is a very important factor in fostering and perhaps provoking attacks, but that is all."

Mental Symptoms.—The *psychic disturbances* are prominent in most cases of chorea; only occasionally are they entirely absent. The *irritability* of the child is characteristic; *violent outbursts of temper* are also frequent; *memory is faulty, and concentration almost impossible.* In the

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severe cases there may be *hallucinations, delusions* and *mania* (Chorea insaniens). Collins and Abrahamson show that 54 per cent of cases had psychic disturbances. Dementia does not develop or follow simple (non-huntingtonian) chorea.

The prognosis of the psychic disturbances of chorea is, as a rule, favorable, though their duration may be variable and a positive forecast giving a time limit is absolutely impossible.

Sensory Disturbances.—The disturbances of sensation are only rarely prominent. There are occasional cases in which there are persistingly painful points, numbness, tingling or burning sensation. In some there may be an element of added *hysterical hemianesthesia.* In all of these conditions the symptoms yield as the choreic movements cease—or shortly after.

Motor Disturbances.—Cases in which there is the greatest *motor activity* and *agitation,* those which appear most severe, often terminate very suddenly; while others with little choreic movement and less agitation often drag a weary course.

Latent chorea is slow to recover, and may persist during months with repeated exacerbations in some cases. Langmead is correct in concluding that "the two most important questions to ask in such cases are with regard to sleep and feeding. As long as the child is sleeping well, and can be fed naturally, no untoward result need be feared."

Muscular Weakness.—Muscular weakness associated with or following chorea yields to treatment—rest particularly—and disappears entirely without leaving a remnant.

The weakness may simulate motor paralysis—either *hemiplegia, paraplegia,* or *monoplegia;* it requires accurate differentiation in occasional borderline cases. In all of these a favorable prognosis may be given.

Additional Factors.—Marked *loss of flesh* does not influence prognosis unfavorably. Choreic children are often much reduced by the active movements and sleeplessness but their convalescence is usually prompt, and satisfactory return of weight is the rule. The *involvement of the sphincters* is only present in the terminal stages of the most malignant choreas in which the forecast is exceedingly grave. The *urine* offers no prognostic data.

Eosinophilia in Chorea.—While the examination of the blood of choreic patients offers no data for prognosis, the experience of Macalister, Brown, Cabot, and Leopold tends to prove that eosinophilia is present in most cases of true chorea. The persistence of eosinophilia or its recurrence forecasts a relapse (Leopold); its presence in abnormally high percentage (children normally show slight eosinophilia) is proof of incomplete cure. Absence of eosinophilia according to Leopold "may prove of some diagnostic significance in borderline and doubtful cases and has, therefore, a relative prognostic value."

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Heart.—Cautious observation and physical examination reveal heart anomalies in most cases of chorea. These may be either functional or organic. The *irritable, erratic,* and *tumultuous heart with overactive systolic force is characteristic of chorea. Systolic murmurs* are common, as are *changes in the size of the heart.* It is often difficult to decide whether there is endocarditis or only functional anomaly. Unquestionably endocarditis, occasionally pericarditis, are responsible for the physical signs in a large proportion of cases, and materially influence prognosis.

Endocarditis is almost constantly present in fatal cases of chorea. Osler says *"There is no known disease in which endocarditis is so constantly found, post mortem, as chorea; it is exceptional to find the heart healthy."*

In those who have had chorea, Osler's contention is correct that "the primary heart trouble in chorea is in a majority of cases, at least, an endocarditis." In most of these cases the cardiopathy continues during life without causing secondary disturbances, often but faint physical signs. 51 3/7 per cent of 140 cases examined from 16 to 2 years after the cure of chorea, showed evidences of a damaged heart.

The majority of *endocarditides* associated with chorea in young girls, however loud the murmurs or persistent the physical signs during the progress of the disease, yield to treatment with the disappearance of all subjective symptoms; about the time of puberty there is but faint remnant of the previous endocarditis in physical signs, though thorough examination shows a slight cardiopathy. The complication of *pericarditis* influences prognosis unfavorably.

Gibson has shown the frequent presence of pericarditis with and without endocarditis in fatal cases of chorea and polyarthritis, while Osler in his oft-quoted monograph reports "in 19 of the recent autopsies in chorea which I have collected, pericarditis occurred as a complication, and in 17 it was associated with endocarditis." *Myocarditis* with endo- or pericarditis, the presence of which is made positive by physical signs of cardiac insufficiency, offers an exceedingly grave outlook. Poynton has called attention to the persistence of tachycardia associated with chorea and the progression of mitral stenosis.

In most of my cases of chorea fatal endocarditis with pericarditis was of rheumatic origin. *Typical mild chorea minor* without serious complications, with the "choreic heart" and usual motor and psychic symptoms runs a favorable course when cautiously watched and treated in from seven to ten weeks. The *severe cases* may persist with or without remission during from four to seven or eight months.

Special Considerations

Improvement of the psychic disturbances is usually promptly followed by the gradual cessation of the involuntary movements.

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The *mortality* of chorea is between 2.5 and 3.5 per cent. Wollenberg places it at 3 per cent. Endo- and pericarditis are the leading causes of death in most cases. The prognosis of chorea at puberty or shortly before is less favorable than between the sixth and tenth year.

Chorea in the aged is a formidable disease. I have rarely found it primary. One of my cases was associated with diabetes mellitus in a man seventy years of age. As a rule it will be found, as already suggested elsewhere in this article, that cautious diagnosis will prove the great rarity of adult, particularly senile chorea.

There are occasional *foudroyant cases* associated with deep involvement of the sensorium, febrile movement, uncontrollable insomnia, heart lesions (endocarditis) which run a rapid course to death in from five to twelve or fifteen days.

A similar rapid and unfavorable termination may occasionally follow or be associated with scarlet fever, diphtheria, or typhoid fever.

Relapse is frequent and must be expected in about fifty per cent of all cases. With our appreciation of the infectious nature of the disease, the search for the infecting focus, and its removal, relapses will be less frequent in the future. Females are more subject to relapse than are males. Relapses in males rarely follow the third, while females may have as many as twelve to fifteen.

The severity of succeeding relapses is progressively reduced, as is also the duration (See Reports; 139, 80, and 55 days as the duration of the first three attacks respectively—Church and Peterson). *The interval between remissions* is variable; the average in my cases was between ten and thirteen months. The condition of the heart may remain unchanged with succeeding attacks. In some cases there may be no positive evidences of heart involvement during the first attack but subsequent attacks usually show positive "choreic heart," evidences of endocarditis, or chronic cardiopathy.

There are subacute and chronic cases of chorea; the majority of these finally recover, though it should be remembered that occasional chronic cases with remissions and exacerbations may continue during several years. There are but few cases in which uncomplicated choreic disease persists indefinitely.

Recurring chorea and the endocarditis, or functional disturbances of the heart which accompany it, interfere very materially with the *education and development of the child.* Such children are handicapped in spite of the fact that many choreic children, girls particularly, are unusually bright. Cases of tic are often mistaken for chorea in adults, and this fact should be remembered in diagnosis and prognosis (See Tic Convulsive).

Complications other than those mentioned are exceedingly rare, and prognosis is easily made in connection with the study of the heart anomalies.

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Huntington's Disease (1872)

(Huntington's Chorea, Chorea of the Aged, Family Chorea, Chronic Progressive Chorea, Acute Hereditary Chorea)

Huntington of Long Island has received the credit for calling the attention of the profession to a variety of chorea which he found among a number of families in south-eastern New York, in whom for years his father and grandfather had observed the patients who were known as "shakers." Waters in 1842, and Lyon in 1863, both reported authentic cases of hereditary or chronic progressive chorea before Huntington's article appeared (1872). The disease proved to be hereditary and was easily traced through several generations, *attacking more victims than any other familial disease* in the individual families stricken—at times one-half the entire family. The disease does not reappear after the "hereditary chain" is broken (Church and Peterson); hence it does not skip a generation. Males are more frequently attacked than females.

Chronic chorea presents positive histopathologic changes and ought not to be classified pathologically with true Sydenham chorea. The most marked changes are found in the basal ganglia, and the lenticular and caudate nuclei. "The lesions consist principally in large accumulations of

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neuroglia cells, fiber degenerations, and considerable cell destruction. The quantity of products of disintegration in the basal ganglia is augmented as a result of the parenchymatous changes" (Dynan). Dynan gives a full report of eight cases of chronic progressive chorea; of five cases tested, the Wassermann reaction with the blood serum "was negative, and examination of the cerebrospinal fluid in one case for Wassermann reaction was also negative, its appearance clear, protein content not increased, and there were only four cells per cmm."

It is not a disease of early life and appears after the thirtieth year, usually between the thirtieth and the forty-fifth year, though it may develop later in life. The prognosis is absolutely bad as can be readily concluded from the "three marked peculiarities in this disease:

1. Its hereditary nature
2. A tendency to insanity and suicide
3. Its manifesting itself as a grave disease only in adult life."

Huntington in his graphic rehearsal of the course of the disease accented the fact above mentioned that "if by any chance these children go through life *without it* (the disease), the thread is broken, and the grandchildren and great grandchildren of the original shakers may rest assured that they are free from the disease."

There are no recoveries from true Huntington chorea recorded; neither are the symptoms relieved, but they gradually increase after beginning as does ordinary chorea. Before death, every voluntary muscle of the body is affected. If members of a "shaker family" live beyond the fortieth year without chronic symptoms, the chances are that they will escape the disease.

The duration of the disease may be twenty or more years—some of the patients have reached the age of seventy. Death may follow extreme *marasmus* with *dementia,* acute *intercurrent infection,* or *suicide.*

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Dubini's Disease

(*Electrical Chorea*)

Dubini in 1845 described a disease which he found in the malarial districts of Italy which does not resemble true chorea; it has some earmarks of myoclonus and hysteria as well. It is without known pathology. Infection of some kind—malaria, tuberculosis, meningitis—may precede or accompany the disease. The disease derives its name "electrical chorea" from the fact that the extremities suddenly show contractions (spasms) as if responding to an electrical stimulus, though the electrical reactions are normal. There is no loss of consciousness during the spasm which often recurs with considerable regularity, and may simulate epileptic convulsions (without loss of consciousness). There are as a rule so sensory disturbances, though the skin in occasional cases may remain hypersensitive during a short time. There is in almost all cases progression during from three to five months; the convulsions recur at shorter periods as the disease advances until finally the status epilepticus persists. Death follows in coma. In a few cases there have been remissions, but these are usually followed by exacerbations and continuous symptoms.

6. *Tetany*

(*Tetanie, Tetanilla, Intermittent Tetanus*)

See Disease of the Parathyroid Gland, Section X, V, I

7. *Epilepsy*

(*Falling Sickness, Morbus divinus, Morbus sacer*)

General Considerations.—Epilepsy is a paroxysmal disease characterized by the irregular recurrence of general convulsions, which usually involve the entire body, associated with loss of consciousness in its typical and most frequent form (*grand mal*). There are cases in which there is only an evanescent—fleeting—loss of consciousness without general convulsions, or the convulsive movements are so slight as to remain unnoticed. These are the "smaller attacks" (*petit mal*). Both of these types are known as "true" or "genuine" epilepsy, also "essential" or "idiopathic" epilepsy, and are of primary origin so far as we know at the present time; they are without known pathologic fundament.

The *"epileptic equivalents"* consist of "apparently volitional or coördinated motor or mental actions during a state of modified consciousness" (Herter-Clark) ("psychical epilepsy," "psychical epileptic equivalent"). These lapses with motor, sensory, visceral and psychic manifestations, may and usually do substitute minor attacks (grand and petit mal). In con-

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sidering the prognosis and diagnosis of epilepsy it should be remembered that one form of "essential epilepsy" may merge into another, or different forms may be combined in the same subject; or in occasional cases after a period of grand mal, years of petit mal may follow without more than an occasional grand mal or none at all, or after varying periods of alternation of the grand and petit mal, psychical epilepsy may follow. There are no possible data by which the clinician can forecast, with any degree of certainty, the vagaries of the disease. It may be assumed with considerable positiveness that minor attacks are interspersed, which are so fleeting as to escape recognition in many chronic cases, and that the recurrence of *nocturnal and modified attacks* of grand mal, in which the tongue is not bitten, frequently remain unnoticed.

In the acceptance of "the anitopathological study in the epileptics," according to Pierce-Clark, "we now recognize more and more that true epilepsy is a real cortical disorder of which the fits are but one of the psychic incidents, and that the seizures should no longer usurp the whole field of attention with their special and specific therapy of sedation."

Focal or jacksonian epilepsy is secondary and dependent upon *focal and organic lesions;* the convulsive movements are limited, and localization of the lesion in the motor (cortical) area is, as a rule, possible.

Epilepsy, therefore, may be considered to be of (a) *primary* or (b) *secondary* origin.

The epileptic convulsion may be an expression of a disease *per se* of which the explosive seizures are the leading symptoms, or the seizures in the "epileptic" individual may prove to be symptomatic of one of many conditions. When epileptic seizures recur on slight cause in the subject of chronic epilepsy, it must be assumed for our purposes that the cortical cells are ready for an explosion and that the underlying and important factor remains the instability of the cortex or the subcortical tissue, and this we are unable to eliminate, though we may in some cases partially control the exciting factors.

The Primary Epilepsies are:

(I) Major Epilepsy (Grand Mal)
(II) Minor Epilepsy (Petit Mal)
(III) Psychic Epilepsy or Epileptic Equivalents.

Secondary or focal epilepsy, jacksonian epilepsy.

(a) The Primary Epilepsies

The *epileptiform seizures* which are toxic, of traumatic or reflex origin, due to cerebral lesions (outside cortical area), heart lesions (Adams-Stokes), or uremic lesions, are not included among the true epilepsies, neither does so-called "hystero-epilepsy" deserve consideration in this con-

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nection. I naturally exclude from consideration epileptiform conditions associated with the meningitides, encephalitis, fractures, tuberculous sclerosis of Vogt, hydrocephalus, brain tumor, and disseminated or localized cerebral or cerebrospinal syphilis.

Convulsions in children due to reflex disturbances, teething (?), worms (?), and other questionable causes, are not epileptic and are considered separately.

In establishing the *pathogenesis of epilepsy* the consensus of opinion favors the cortex as the starting point of all essential epilepsies. For prognostic purposes the result of experimentation may at the present time be accepted which proves that *cortical irritation may cause all of the phenomena of the genuine epileptic seizure.* Cortical irritation being, in the large proportion of cases aggravated or produced by toxic agents, the prognosis of the individual case of chronic epilepsy, must be favorably influenced by the control of such factors as act directly or indirectly as cortical irritants (alcohol, syphilis, lead, mercury, morphin, chloroform, ether, circulatory anomalies resulting from excess, overwork, and a variety of other controllable factors).

Factors Which Influence Prognosis

Age.—No age is exempt from epilepsy, though most cases are found during early life. Oppenheim's material proves three-fourths of his cases to be below the age of 20. Osler reports 460 cases of epilepsy in children, of which he recorded the ages of the initial paroxysm in 437:

First Year	74
Second Year	62
Third Year	51
Fourth Year	24
Fifth Year	17
Sixth Year	18
Seventh Year	19
Eighth Year	23
Ninth Year	17
Tenth Year	27
Eleventh Year	17
Twelfth Year	18
Thirteenth Year	15
Fourteenth Year	21
Fifteenth Year	34

The prognosis is most unfavorable for control in those cases which begin before the age of ten years. "Infancy and puberty are the most dangerous periods for the appearance of the disease" (Munson). Turner

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holds that cases which begin at puberty offer a more favorable prognosis than do those younger. From 20 to 35 years of age the prognosis is bad. The average age at death at Sonyea (Craig Colony) was 30.08 years. The largest number of deaths at any one age was at 19; 50 per cent of the deaths were between 15 and 25 inclusive.

With the increase of *arteriosclerosis, "senile epilepsy"* is more frequently met than formerly. *Epilepsy which shows its first symptoms after the fortieth year with evidences of vascular or cardiovascular changes offers an unfavorable outlook.* Most of my senile epilepsies in which the symptoms were characteristic died in coma after shortening of the intervals between the attacks, often preceding evidences of dementia and the gradual development of the *status epilepticus.* Some of these patients have died of *apoplexy, angina pectoris, myocardial insufficiency* (suddenly)—rarely rupture of the heart (only one).

Heredity.—Heredity, in spite of the contentions of many able authorities remains an important factor in epilepsy. Statistics upon this point are contradictory, but the weight of authority is in favor of the overpowering influence of heredity in the causation, either directly or indirectly of the symptom complex. The experience of Gowers proves direct heredity in 35 per cent of his cases. Osler's statistics include 435 cases; 5 only in which the epileptics were children of epileptic parents, and in these the disease was traceable to the mother in every instance. He says "in my list there were only 31 cases in which there was a history of marked neurotic taint, and only 3 in which the mother has been epileptic."

My experience establishes hereditary factors as exceedingly important in epilepsy, and the prognosis has been unfavorably influenced in the children of epileptics, the insane, neurotics, alcoholics or those otherwise handicapped by vicious habits or blood taint.

It is not unusual to find several children in the same family afflicted; in these, the control of the paroxysms is often difficult or impossible. *The most unfavorable cases in my experience have been found in the offspring of neurotics, epileptics, or those with other chronic disease of the nervous system with the history of alcoholism.*

Clark in a recent article presents views which deserve space in this work. He holds that if we conclude that epilepsy "would seem to be dependent upon certain unknown complex hereditary factors producing a form of cortical or subcortical instability upon which a variety of endogenous toxins may act, causing the disease," we may hope that a therapy may ultimately be established as the result of further experimentation and the thorough study of metabolic processes in cases of this disease, which will lead to better results than we have obtained in the past. Clark emphasizes the fact that "hereditariness is no bar to recovery from epilepsy. Indeed it would seem to be for a good prognosis rather than against it, as shown by numerous studies, and especially my own data, where two-thirds

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of the recoveries were recruited from the hereditary cases." Clark further quotes Southard's contention. He adds "Not a little light is thrown on the reason why the hereditary epilepsy recovers, if one accepts Southard's contention that the hereditary factor is *permissive* and not *mandatory* for the occurrence and continuance of epilepsy in the descendants of neurotic family stock."

It is possible that in the individual "hereditary" case which can be thoroughly and continuously safeguarded, much can be done to overcome exciting factors by the study of the metabolic processes and habits of the patient and their scientific regulation; hence the warning given by the hereditary tendency may influence prognosis favorably. The history of heredity in uncomplicated cases of epilepsy "does not necessarily militate against the prospects of arrest or improvement in any given case."

Sex.—Sex exerts no influence on epilepsy or its prognosis. At the Craig Colony "the proportion of males and females dying is practically the proportion admitted, though the males are very slightly in excess" (Munson). Spratling in 68,040 cases in this country and Europe found 36,865 males and 31,175 females.

Alcoholism.—Alcoholics not infrequently develop epilepsy, and the prognosis is unfavorably influenced by the chronic secondary changes due to the long continued poisoning. As already mentioned, alcoholism in the parent unfavorably influences epilepsy in the offspring.

Syphilis.—Syphilis may cause epileptiform convulsions. *The majority of these cases are probably dependent upon positive pathologic change,* which with radical treatment, leads to recovery.

Syphilitics who are also of neurotic habit, who are burdened with an unfavorable heredity or whose habits are vicious, may without definitely demonstrable lesions develop epilepsy during the secondary period. The prognosis of such cases is not altogether bad. Under treatment and control from 10 to 20 per cent of such patients are relieved. *It should be remembered that the majority of syphilitics who develop epileptiform symptoms suffer from syphilitic disease of the brain, and are not true epileptics.*

Traumatism.—When traumatism causes epilepsy there is usually a focal lesion which may be localized, in which event the treatment is likely to be surgical; the epilepsy is secondary, and the prognosis depends entirely upon the ability of the operator to remove the cause. Such cases are likely to be of the jacksonian type and are separately considered.

Epilepsy (true—grand or petit mal) may follow trauma without demonstrable lesion in focal symptoms. In these cases the usual symptom complex of essential epilepsy is present. The trauma simply proved to be the exciting factor. The prognosis of most of these cases is the same as all others without known anatomic lesion.

I have elsewhere (*encephalitis, cerebral hemorrhage,* etc.) considered cases of *posthemiplegic epilepsy*—in all of these, in spite of the

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return (usually partial) of motor power, the epileptic complex continues but little influenced by treatment, as a rule uninfluenced entirely; but rarely do the convulsions cease after years of recurrence.

Sunstroke.—Epilepsy occasionally follows sunstroke. Such cases are unquestionably due to organic change—meningo-encephalitis, etc.—and remain practically uninfluenced by treatment in my experience (See Sunstroke).

Fright—Acute Infections, etc.—*Epilepsy may remain dormant or unrecognized during long periods—even years.* In such cases an insignificant factor may prove sufficient to light the case to activity, *fright, sudden emotion, long continued worry, prolonged masturbation or other venereal excesses,* and *acute infections* (typhoid) are included. It is not likely that in the normal subjects—those with average resistance—these alleged causes, usually without effect, produce the disease; when they do, it will be found that there is the *"predisposition," evidences of degeneracy* often with an *abnormal heredity.* These cases offer the average prognosis of the disease.

Diet.—*Diet* will always remain one of the most important factors in the prognosis of epilepsy, for the majority of cases show faulty metabolism. "The theory by which cures or arrests are brought about is rather unsatisfactory speculation. Nevertheless the whole successful plan of hygienic treatment speaks very favorably for the preconceived idea that the disorder in most cases is a metabolic one, and a setting right of the personal habits and plan of living restores the patient to a stationary state equal, if not superior, to his health before epilepsy began" (L. Pierce Clark).

Pregnancy.—The Germans and some English authorities hold that pregnancy exerts a favorable influence on epilepsy. This is not proved by the examination and thorough consideration of a large material. It is safe to conclude that gestation has but little influence upon the disease. Turner says "At the best there may be only a temporary respite, but pregnancy is the forerunner of the puerperium, a period which is especially prone to epileptic attacks." "There are three periods when epileptic fits were prone to develop: at quickening, during the first few days of puerperium, and during lactation."

Ocular Anomalies.—It is questionable whether cases which yield to the correction of ocular anomalies (strain usually)—and some do—are essential epilepsies. The fact remains that these cases cannot be differentiated from genuine epilepsy. The number which yields to the correction of ocular defects is small—in the large majority of cases of true epilepsy such treatment has, in our experience, proved futile.

Amblyopia, etc.—In considering amblyopia and other ocular symptoms it should be remembered that *temporary amblyopia,* involving both eyes, occurs in certain functional diseases of the brain, particularly in epilepsy and migraine. In both of these conditions the loss of sight is

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always transitory and paroxysmal. In epilepsy the loss of sight usually precedes the convulsion. No permanent blindness need be feared.

BABINSKI PHENOMENON.—In the prognosis of epilepsy and *epileptoid disease,* for which accurate differentiation is imperative, the *persistence of the Babinski phenomenon after the seizure, during several hours, is proof of symptomatic epilepsy—usually hysteria and not true epilepsy;* the prognosis is usually correspondingly good. The phenomenon disappears shortly after the attack.

DISORDERED NUTRITION.—Disordered nutrition is responsible for the recurrence of paroxysms in many cases of grand mal—a fact which is corroborated by urinary examination. It has been found that intestinal putrefaction is closely related to the explosive seizures of epilepsy. Under these conditions there is evidence in the urine of a disturbance of the normal relation between the "preformed and the combined or ethereal sulphates in the urine 10-1)" (Herter and Clark). The persistent presence of indican (indoxyl sulphate) in the urine of epileptics is striking in a large number of cases. There is a decided increase of these substances just before and during the epileptic fit to be decreased immediately after. The ability of the therapeutist to influence intestinal fermentation by treatment, with the removal of the ethereal sulphates from the urine, exerts a wholesome influence in decreasing the number of paroxysms in some cases. The release of a troublesome *phimosis* has occasionally relieved *epileptoid conditions* which could not be differentiated from epilepsy. The surgical treatment of a peripheral local irritation has in rare cases produced the same favorable result (cicatrices in peripheral nerves, etc.). Such cases naturally cast a suspicion upon the diagnosis.

(*Course of the Disease*)

Epilepsy which originates during scarlet fever (most frequent), typhoid, measles, smallpox, influenza, pertussis, malaria, which follows meningitis, prolonged labor or forceps delivery, is not easily controlled—rarely entirely overcome. It may be concluded that the acute infections often exert an inhibitory influence on the convulsions. After convalescence but few cases continue to show any wholesome effect from the added infection (Turnowski).

The *aura* bears no relation to the severity of the attack in most cases. The absence of an aura has been noted in both mild and severe epilepsies. I have found a number of cases in which the absence of the aura proved alarming because of the sudden severe convulsion without warning serious bodily injury resulted. In one of my cases a molder was burned by the melted iron which he was pouring. In a number of cases the warning, i. e., the aura, may protect against injury. One of my cases, a street car conductor, is always able to foretell the approach of an attack two

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hours before its outbreak by a peculiar "bandlike" sensation about the head which makes it possible for him to call his substitute and reach his home where he protects himself against injury by getting into bed.

The ability to abort the epileptic seizure by pressure of an extremity when the aura begins in a hand or foot is possible. Such efforts are not always successful in the individual case. Convulsions which recur at short intervals, are severe, and continue beyond the average duration which are associated with long periods of stupor and final *amnesia* (forgetfulness), are evidence of progressive degeneration. Such cases are likely to develop *dementia. Loss of self control, confusion of intellect* shortly after the convulsion, a desire "to get away" may recur for years without material advance toward complete mental alienation. One such case, a woman, now under treatment, age thirty-four, has continued since early childhood to have periods of delirium and passionate outbreaks in which she is belligerent, without the slightest evidence of mental unbalance during the interval between attacks; in fact she continues unusually bright and cautious in the handling of her affairs.

The development of *active mania with homicidal tendencies* may follow the attack and continue in some during periods varying from a few hours to several days. Such symptoms recur and are often uninfluenced by treatment. Cautious surveillance alone prevents the destruction of life under such conditions. *Epileptic delirium* may recur at short intervals, and offers an unfavorable prognosis for control. Cases in which convulsions of the grand or petit mal type recur at short intervals are likely to continue *lethargic mentally;* they remain uninterested in current events and often become confused during long periods. Such cases may show long periods of improvement under treatment and rest, but the chances are that eventually, unless there is some acute complication which terminates life, the mental deterioration will progress to the full development of *epileptic insanity.* Cases in which delirium or mental disturbance follow the epileptic fit usually clear in the course of a few hours; the same is true of motor weakness and sensory disturbances, as a rule. Paretic conditions of one or more extremities in individual cases (non-jacksonian) yield to rest and time—often in a few hours or days.

I. Grand Mal

Dislocation of the humerus is an occasional complication of grand mal. One of my cases lived to be sixty-five years of age; during fifty years of his life he had epilepsy, and for twenty years had grand and petit mal. In all attacks of grand mal he dislocated one or both humeri always requiring ether anesthesia for reduction; the quantity of ether used was enormous. Mental lethargy finally followed, and he died in the status epilepticus.

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The postepileptic period is not as a rule associated with danger to life. I have never seen a death following closely upon epileptic seizure in which there was not some added complication. The majority of epileptics are more or less affected by the seizure. They appear lethargic, somnolent, without their normal energy. This condition does not in average cases continue beyond three or four hours. In some cases the patient falls into a deep sleep from which he is aroused with difficulty, and immediately falls asleep again. The majority of patients are fatigued after their experience in spite of the period of sleep.

A small proportion of cases seems unaffected mentally and physically by the attack. Once over, they are again bright and ready to go on with their work; the majority of these belong to the "petit mal" class. The thread of conversation or line of work may not be interrupted; without the break of a sentence I have seen these patients resume as if nothing had happened.

Nocturnal epilepsy, as already suggested, may persist during many years, often so mild as to escape detection. This variety of epilepsy may not materially influence the general condition of the patient or interfere with his activities, until as usually happens, there are diurnal attacks and the patient often falls into a somnolent condition during unusually long periods following the convulsion. At times without added symptoms I have seen these patients in semi-coma for days; pulse but slightly accelerated, and entirely without fever. Such cases are not easily influenced by treatment, and the majority of chronic nocturnal epileptics have finally died in the *"status epilepticus"* or from pulmonary tuberculosis.

The *"status epilepticus"* is a condition in which epileptic seizures follow in such rapid succession as to continue unconsciousness almost without interruption. This condition continued beyond thirty-six to forty-eight hours is of serious import. Such patients gradually fall into a deep and uninterrupted coma in which they usually die. With the persistence of high temperature the prognosis is bad and the duration short. There are no criteria which make it possible to foretell the length of the interval between attacks. In the same subject, convulsions may follow each other in rapid succession; may sometimes recur many times during a single day; and may not recur for months or even years thereafter. It is not uncommon to find epileptics free from all symptoms without the slightest suggestion of the disease during such long periods as to lead both the patient and physician to the conclusion that the disease is under control, when without warning or known cause there is a fresh outbreak. If there is any regularity in the time of the recurrence of convulsions, as during menstruation in women, rest and treatment may postpone the explosion.

Grand mal in chronic cases may be expected to recur in the average uncontrolled case once or twice each month.

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(II) Petit Mal

All authorities are agreed that the prognosis of the smaller attacks—petit mal—is less favorable for control than is that of grand mal. There is great danger of bodily injury in those cases in which sudden vertigo throws the victim without warning. The minor attacks are not so easily influenced by drugs as are the larger. The ability to arrest or influence the frequency of the attacks was studied by Turner, who found that 49 per cent of grand mal, 35 per cent of combined grand mal and petit mal, and only 26 per cent of petit mal were influenced by treatment.

(III) Epileptic Equivalents

Psychic epilepsy is exceedingly rare. Of 1,325 cases of epilepsy collected by Spratling at Sonyea, only 4 were of this type. The prognosis is best in those cases without early or evident intellectual weakness or without "striking intellectual aura."

My experience has been that the psychic equivalent in essential epilepsy appears only at long intervals in most cases. One of my cases became an epileptic automaton during which he traveled far from home after suddenly disappearing, and was found wandering uninjured in a large city where he had taken a room in a leading hotel without exciting the slightest suspicion. This man lived many years after this occurrence; he had repeated grand and petit mal and finally died of intercurrent disease.

All cases of suspected psychic equivalents demand close study that a forecast may be given of the existing mental status, and it should be remembered that *such patients may, if unguarded, execute major crimes of which they have no knowledge and for which they are not responsible.*

(b) Secondary or Focal Epilepsy—Jacksonian Epilepsy

(Hughlings Jackson, 1869)

General Considerations.—Jacksonian epilepsy belongs within the domain of the surgeon. It is due to a positive and localizable lesion and if within the reach of the knife, unless of long standing, offers at least the possibility of cure. Jacksonian epilepsy may, in advanced cases, alternate or be complicated with either grand or petit mal, usually the former. Long continued grand mal with primary jacksonian convulsions offers an unfavorable prognosis for any treatment—medical or surgical.

Frequent and full references to the epileptic syndrome and to jacksonian epilepsy are made in the chapters on brain tumor and other organic diseases of the nervous system, to which the reader is referred (See Index).

Epilepsy, when a complication of *meningitis* or *meningo-encephalitis*

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or dependent on these causes, offers an unfavorable prognosis for relief of the convulsions. The convulsions are frequent in the paralyzed limbs, besides being general.

With added organic disease of the nervous system I have seen epilepsy disappear entirely, change its form from the grand to the petit mal type, or continue uninfluenced. I have recently in dispensary practice seen two cases of tabes dorsalis in which with the advance of the latter disease, epilepsy which had existed since early childhood of the grand mal form, was found to have been relieved and only an occasional "wave" of petit mal was noticeable.

The examination of the *cerebrospinal fluid* withdrawn by lumbar puncture offers no prognostic data.

The Blood.—Fackenheim at the recent Congress für Innere Medizin (1914) concluded that before the attack there was a marked reduction of hemoglobin, the destruction of both red and white corpuscles, and these conditions with increased coagulability of the blood he believes are of diagnostic and prognostic value. His observations have not yet been confirmed. The large mononuclear lymphocytes are increased before the attack. There is poikilocytosis and microcytosis during the attack.

Course of the Disease.—A small proportion of epileptics die from *injury during the attack*, a few are drowned, and an occasional victim commits suicide. It is surprising that there are so few serious accidents when the large number of epileptic fits from which many suffer are considered. The tongue biting does not as a rule inconvenience the epileptic long, as the organ heals promptly.

Epilepsy itself—directly—rarely causes death, but those who have had the largest experience with the disease recognize its menace, and are agreed with Munson of the Craig Colony when he says "Our experience at the Colony is that the disease carries with it very grave dangers; the span of life is shortened and there is a special liability to certain diseases and to traumas."

Complications.—*Pulmonary tuberculosis* is the most frequent cause of death. Munson in his conclusions holds that "the causes of deaths in epileptics are quite largely associated with the disease itself and may be divided into two main groups: pulmonary conditions, and conditions of a purely epileptic character."

Pulmonary edema may develop during the attack; Shanahan has reported such cases. The prognosis of these is exceedingly grave.

Pneumonia following the attack in which the patient was neglected has been a cause of death in a number of my hospital cases. In Munson's material there were 142 cases of pneumonia; these cases were not neglected during the attacks, but were under surveillance.

No epileptic during the attack is free from danger, for death may suddenly follow from causes already mentioned (particularly trauma,

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asphyxia, edema) *and a number of deaths will occur without apparent cause.* These facts justify a better prognosis in those cases which are cautiously guarded and nursed.

General Conclusions.—The *general condition* of the epileptic varies with different types of the disease, and is influenced by a variety of causes. While many epileptics appear to be in good general condition, the disease is likely to undermine resistance. There is gradual loss of strength until the average epileptic is below par almost continually, and life is materially shortened indirectly by the disease.

If a patient has remained without attacks 9 years (Turner) it may be concluded that he is cured. Sinkler observed only 4 cases of relapse out of a total of 24 after 9 years' remission. In one case there was a remission of 27 years with final recurrence. Spratling believes that the time limit of Turner is too long, that "a person may be cured of epilepsy and then have it again." I would recommend the longer period for prognostic conclusions, and would argue against the assumption that an epileptic who showed recurrence had been completely cured.

Spratling after an experience of 14 years in the daily care and treatment of 1,800 cases of epilepsy in persons of all ages, reported 34 cures, and concluded "that epilepsy is curable in from 5 to 10 per cent of all cases." Spratling holds that "the failure to secure better results generally in the treatment of this disease must frequently be laid to the failure to treat the individual and his disease as a unit and to treat them both along the very broad, comprehensive, and unyielding lines they both require."

The prognosis before the introduction of the bromid, now unquestionably used at some time in the treatment of almost all cases, does not differ materially from that of today. Turner mentions in the *pre-bromid days* Hufeland's cures of 5 per cent; Russell Reynold's 10 per cent; Trousseau 20 cures in 150 cases, or 13 per cent; Herpin 19 cures in 38 cases, 50 per cent (questionable). Post-bromid days: Nothnagel 5 per cent of cures; Laehr gives 6 per cent; Ackerman 7.6 per cent; Dana 5 to 10 per cent; Wildermuth 8.5 per cent; Habermas 10.3 per cent and Alt gives 12.5 per cent. Volland reports 4,215 cases observed, of which 245 were discharged cured. R. Stern reports an unusually large percentage of cures.

Cases which are influenced favorably by the bromids should show no mental torpor, marked improvement from doses which remain without disagreeable constitutional effects, and should not fall into the status epilepticus when the remedy is withdrawn.

Boekelman has reported cases in which the withdrawal of the bromids has precipitated the epileptic state. I quote from Clark: "To my mind, the introduction of special medicaments of sedation in the epilepsies has been fraught with more harm than good. The sedatives have clouded the issues of causation and prognosis to a remarkable extent. They have dis-

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located and cloaked the errors of metabolism in the epilepsy problem without giving commensurate aid. I decidedly take issue with Féré's and Turner's views that the introduction of the bromids has aided the prognosis, especially as regards permanent cures. The bromids mask the progress of the disease and make a full understanding of the forces at work in the individual case almost unbelievably complex. I have seen many patients treated by sedatives steadily advance in physical, mental and moral deterioration in the face of a steady cessation of fits—suppression of fits is squared by an outburst of status epilepticus or a furious maniacal outbreak."

Cases which are favorably influenced by treatment, as a rule, show marked decrease in the number of convulsions during the first year of continuous treatment (50 per cent).

The least favorable cases are those of acquired or congenital mental anomalies with any of the forms of epilepsy.

Surgery has been unable to materially influence the prognosis of essential or idiopathic epilepsy. Cases which are amenable to surgical treatment must be of focal origin, usually jacksonian. Epilepsy dependent on a discoverable lesion offers a better prognosis than does the true epilepsy, and should not be considered in the same class.

The clear statement of Hippocrates in his Prognostics shows that scant progress has been made in the treatment or cure of the disease since his day—twenty-five hundred years ago. He wrote: "If the Sacred Disease attacks little children the greater number die. If youths and young adults, recovery may take place but there is danger of its becoming habitual and even increasing, if not treated by suitable remedies. Such also is the case when it attacks children. When it attacks people of advanced years it often proves fatal. When a person has passed the twentieth year of his life the disease is not apt to seize him, unless it has become habitual from childhood. When the disease has prevailed for a length of time it is no longer curable."

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8. *Migraine*

(*Hemicrania, Sick Headache, Blind Headache, Bilious Headache*)

Migraine is a *painful, paroxysmal affection,* characterized by headache —usually confined to *one side* of the head—associated with all kinds of *nervous* and *dyspeptic symptoms;* often aura early during the attack with *anorexia, nausea, vomiting, ocular symptoms;* at times *motor weakness* and *sensory anomalies;* often suggestive manifestations of *faulty metabolism, vascular spasm* and *irritation* or *paralysis* of the *cervical sympathetic.*

Migraine does not lead to death; pathologic investigation has therefore been impossible. There are no evidences that the complex is dependent upon organic change, but a strong and justified suspicion that the disease is a neurosis dependent in over 60 per cent of cases upon *heredity;* that in most cases *the exciting factor of the individual paroxysm* is either *fatigue in the non-resistant, error of diet, ocular strain, sexual excess, sudden psychic disturbance, or some toxic condition dependent upon gastro-intestinal upset or faulty metabolism.*

Influencing Factors.—*Heredity.*—Ulrich's statistics relating to heredity are exceedingly interesting. He finds: *positive hereditary influence* in 64 per cent, *probable hereditary influence* in 25 per cent, *absence of hereditary influence* in 11 per cent.

In his hereditary cases he traced the complex to the mother in 74 per cent of 147 cases (106 women and 41 men); to the father in 17 cases—9 per cent (9 females and 8 males); to both parents in but two of his cases (one male and one female). In 24 cases—12 per cent—several brothers and sisters had migraine, and it was not uncommon to find the disease

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transmitted through three generations. In some cases one or more generations may be skipped.

Traumatism.—When migraine follows traumatism it may be assumed that it is a part of a traumatic neurosis or hysteria, or if it persists, it is due to organic disease, therefore symptomatic.

Infection and Other Toxic States.—Cases of migraine which have followed infection or other toxic states are not uncommon. In some of these, the lowered vitality in the predisposed was the exciting factor. In some, the disease continues during many years uninfluenced; in a small proportion of cases with the general improvement of the patient the paroxysms recurred at longer intervals, and finally ceased entirely.

Tuberculosis.—The association of migraine and tuberculosis (Moebius, Ulrich and others) has been noticed. Prognostic data are hardly justified by such association. The prognosis of the infection is, however, scarcely influenced by the occurrence of an occasional migraine.

Additional Influences.—Alcohol, tobacco, lead and *morphin* unquestionably increase the paroxysms, and release from the poisons acts favorably. *Metabolic faults,* as aggravating causes, have long been recognized. Trousseau said: *"Migraine and gout* are sisters." The general improvement of a *gouty* or *diabetic subject* often banishes migraine during indefinite periods. *Patients with goiter—Basedow's disease*—have in my experience been relieved by treatment or operation. It not infrequently happens that chronic *constipation, gastro-intestinal dyspepsia* and *tape worm* have proved causative factors. In such cases the relief of the underlying condition cures the migraine. The *correction of menstrual anomalies* and the relief of *diseases of the genito-urinary organs* improve prognosis, and infrequently lead to cure.

Prognosis during Climacteric Period.—The *climacteric period* is favorable for the disappearance of the complex; indeed, if the paroxysms are not entirely dissipated, it may be safely concluded that they recur at longer intervals, and when persistent are less severe. Migraine when it appears during the climacteric period is not likely to persist long thereafter.

Classification.—Gordon considers the following forms of migraine:

(a) Ophthalmic migraine
(b) Hemicrania sympatheticotonica (white migraine)
(c) Hemicrania sympatheticoparalytica (red migraine)
(d) Migraine associated with the epileptic equivalent
(e) Abortive migraine.

(a) Ophthalmic Migraine

In more than 60 per cent of all cases there are during, or just preceding the paroxysm, *disturbances of vision of a sensory character,* which are

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as a rule unilateral. They include *amblyopia,* in some cases *hemianopsia,* in other cases a bright and moving spot limited to one side of the visual field, scintillating (scotoma) or other annoying features (zig-zagging lines, continually moving concentric circles, repeated flashes of light, etc.). With the blurring of sight the vision is partially defective, and there may be—often is—vertigo, nausea and other *motor, sensory* and *psychic phenomena. Complete loss of vision is not present as a rule, but there is a distinctly paroxysmal amblyopia which* is *partial, unilateral* and *transitory.*

With the ophthalmic, as with all forms of migraine in which there are ocular symptoms, unless the latter are dependent on organic disease they are transitory, leave no permanent effect, and are likely to recur with subsequent attacks of migraine.

In some cases *motor weakness* or even *paretic conditions* are prominent during limited periods (few minutes or hours); they disappear without leaving a remnant. Such symptoms may not be present during all paroxysms, but they are prone to recur. Oppenheim has mentioned the transitory occurrence of *cerebellar ataxia* during seizures of ophthalmic migraine. These are without prognostic significance. *Aphasia* may be a prominent symptom (amnesic) in individual cases following or associated with the paroxysm, yielding promptly as the other phenomena disappear; but it is likely to recur with most subsequent attacks. *Marked depression, apathy,* and *visual hallucinations* have in some cases remained annoying, at times preceding the attack, in other cases accompanying or following it.

Gordon has reported cases with marked *psychic disturbances* (confusion, stupor and delirium). I have found a number of such migraines. In all, the symptoms have been transitory and in spite of occasional persistence during several days in severe cases, their disappearance may be positively promised.

The long continued *paralysis of the motor oculi* (at times as long as two or three weeks) finally disappears, and may or may not return with subsequent paroxysms. It will require thorough study of borderline cases that no mistake in diagnosis and prognosis is made in giving to *acute ophthalmoplegia* its significance. It should be remembered that with migraine the paralysis is coincident with the paroxysm, which is always characteristic, with relief from pain as the ophthalmoplegia appears. The ophthalmoplegia of syphilis does not show sudden paralysis; if there is headache, it is present before and continues with the ocular manifestations. These points are of great value for diagnosis and prognosis.

There are a number of ophthalmic migraines which precede progressive paralysis of the insane. Herter and Clark call attention to their history, in all of which cautious investigation clears the horizon. It should be remembered however, that there are *cases of pure and uncomplicated migraine in which during limited periods visual anomalies, slow*

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and hesitating speech, and lapses of memory, may be present. Such symptoms are transitory, and during the intervals there is absolutely no evidence of organic disturbance or subjective manifestations of mental defect. There is never with migraine, progression of any symptoms which resemble those of progressive paresis.

(b) Hemicrania sympatheticotonica (White Migraine) and (c) Hemicrania sympatheticoparalytica (Red Migraine)

Hemicrania sympatheticotonica and hemicrania sympatheticoparalytica are probably due to irritation and paralysis of the cervical sympathetic, respectively (See Diseases of the Sympathetic System).

(d) Migraine Associated with the Epileptic Equivalent

The association of migraine with epilepsy in the same individual is by no means uncommon. Charcot and Féré in France insisted upon the intimate relation of migraine to epilepsy, while Oppenheim and Strohmeyer were equally enthusiastic in Germany in controverting the dictum of the French School.

The more unfavorable cases are those which bear a close resemblance to epilepsy in the presence of aurae with motor, sensory, and psychic symptoms, and attacks which closely resemble petit mal (fleeting). Ulrich's material shows that 99 of 500 cases (20 per cent) were either directly or indirectly related to epileptic conditions. His conclusions must influence prognosis powerfully:

(I) "Migraine may be symptomatic of epilepsy—it may be an epileptic equivalent."

(II) "Both may be present in the same subject independent of each other."

(III) "Eclamptic conditions with characteristic migraine may be caused by acute infections (reflex eclampsia). In these there is not likely to be recurrence."

(IV) "Persistent migraine may finally merge into true epilepsy (Moebius) just as Gowers has demonstrated that repeated syncope may finally prove an inviting factor of epilepsy."

(V) "Migraine may in the presence of epilepsy disappear, just as both conditions have vanished with the development of grave organic diseases of the nervous system (tabes, dementia, etc.)" (See Epilepsy).

(e) Abortive Migraine

Abortive attacks may be interspersed between any of the other varieties, or there may never be severe headache; simply ocular disturbances

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of short duration which do not as a rule interfere materially with the activities of the patient. Some cases may persist during years with slight "blurs" or "balls of fire" or "zig-zagging of lines" with but little or no headache; many of these are relieved permanently by proper attention to ocular or metabolic faults. It happens in some cases that abortive alternate with fully developed paroxysms.

Conclusions

Symptomatic migraine may depend upon syphilitic infection, malaria, uremia with nephritis, progressive paralysis, brain lesions (tumor) and arteriosclerosis with vascular spasm, with or without hypertension. In all of these, the prognosis depends upon the gravity of the causative factor. The *safest prognosis* of migraine is based on the assumption that while heredity is an important factor and supplies the basis for the development of the symptom complex, there is as a rule an exciting cause which with careful search can be unearthed, and while the majority of cases cannot be cured, they may be materially relieved and may continue to live in comparative comfort to old age. With increasing years there is tendency to recurrence at longer intervals, until in many cases there is final complete relief. The possibility of distant causes should not be overlooked. While the eye will claim attention in all cases, there are rare cases (Margulies) in which labyrinthine disease proves provocative, and its relief has a wholesome effect on the accompanying migraine.

The contention of Spitzner that "migraine is due to a constitutional anatomical defect, namely, an absolute or relative stenosis of the foramen of Munro" (Jelliffe), remains without confirmation.

The clinician will do well to consider many causes responsible for what seems predominant in migraine, i. e., vasomotor disturbances, and will prognosticate accordingly.

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9. Occupation Paralyses and Neuroses

The long continued or improper and overworked muscles and nerves of certain combinations used for the performance of special movements may lead to fatigue or paralysis.

Writers' Cramp and Other Occupational Paralyses

The most frequent occupation neuroses is found in writers (*writers' cramp*).

Among the other *professional paralyses* are those of the violinists, piano players, telegraph operators, typewriters, milkers, machinists, drummers, seamstresses, crocheters, cigar makers, hammer and file makers, miners and other occupations including oarsmen and diamond polishers.

The milder cases, which promptly yield with the discontinuing of the occupation present with some pain, paresthesias and anesthesias. There is no marked paralysis, but evidences of a mild neuritis in tenderness along the nerve involved. The muscles are also tender, and *in the more advanced cases* are more or less atrophied.

Myositis and neuritis are probably the pathologic basis of most professional paralysis.

When once established, if the special work which caused the motor weakness is continued, in spite of improvement during periods of rest, the symptoms recur and become chronic. There are but few exceptions to this rule.

In rare cases mechanical appliances bring relief—but this is only partial.

The *symptoms of writers' cramp* (Scriveners' palsy) are either *spasmodic* or *paralytic*. Most cases are spasmodic. By the spasm of the extensor muscles the fingers separate and extend, and the pen is dropped. The spasm of the flexor muscles makes writing impossible; the pen sticks into the paper, and the pain with spasm may affect the entire arm. For a time writers manage by posture and other devices to overcome the spasm, but in the end, if much writing is done, the spasm recurs with increased symptoms and pain.

With the paralytic form of writers' cramp and other occupations, the muscles weaken suddenly while in use, they are relaxed, and the special work becomes impossible.

In most cases the disease does not lead to noticeable *atrophy of the*

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muscles nor to electrical changes. In severe cases there may be increased excitability to both faradism and galvanism.

Writers' cramp usually develops in both arms, when one is used after the other has become troublesome.

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10. Infantile Convulsions

(*Eclampsia infantum*)

Predisposition.—There are children who upon insignificant cause develop fever, and are at once thrown into active convulsions from which they promptly recover—as a rule without damage. Recurrence with every added insult or fresh infection is the rule, until the susceptible and hyperesthetic child lives beyond babyhood. In occasional cases the tendency to convulsions in such subjects persists until puberty. *The spasm of the glottis* (laryngo-spasm—laryngismus stridulus) is without danger in almost all cases. It is likely to recur, particularly in rachitic and underfed children on slight cause.

Causes.—For the purpose of the clinician it may be assumed that *infantile convulsions are symptomatic,* as a rule an accompaniment of acute infection; at times they are due to nutritional faults; in other cases there is a fundament in organic disease of the nervous system (poliomyelitis, meningitis, meningismus, brain tumor, etc.). Toxic states with gastro-intestinal disturbance, worms, uremic poisoning, reflex causes, alcoholism in the parent, rachitis, congenital defects of the heart and thymus enlargement are also responsible. The significance of convulsions in children with these conditions is fully considered separately. The reader is referred to the included sections.

Influence on Acute Infections.—It may be assumed that the *acute infections are unfavorably influenced by added convulsions; the explosive seizure is an expression of the depth of the infection. With malignant scarlet fever* and *diphtheria* children may die in the convulsion, or with *hyperpyrexia* and *cardiac asthenia* they may succumb in coma after the convulsion. The same behavior often characterizes other deep infections. In all cases the rapidity of the pulse (heart weakness) the behavior of the respiratory organs, the duration of the convulsion, the resistance of the child, the presence or absence of respiratory obstruction (cyanosis), and the depth of the stupor, become important prognostic features, while *the nature and extent of the primary disease must always remain the paramount factor in offering a reliable forecast.* Most diseases are not unfavorably

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influenced by the occurrence of the initial convulsion, but usually it may be concluded that the disease itself proves to be of grave import, as a rule, when the infection or the toxemia leads to convulsions.

Conclusions.—*Convulsions in children, while they last, are never to be lightly regarded.* The prompt relief of irritating or inviting conditions favorably influences the outcome. In some cases of infection and in organic disease, it is of enormous importance to prevent recurrence because of possible hemorrhage and subsequent cyst or organic change in brain tissue which occasionally follow convulsions (See separate diseases of the nervous system).

Accurate diagnosis will lead to trustworthy and timely prognosis in most cases.

E. Diseases of the Sympathetic System

Vasomotor and Trophic Disturbances

1. Erythromelalgia

(*Red Neuralgia*)

Characteristic Symptoms.—In 1872 a paper was written by Weir Mitchell describing a peculiar condition to which he gave the following definition: "A chronic disease in which a part or parts—usually one or more extremities—suffer with pain, flushing, and local fever, made worse if the parts hang down."

Mitchell called attention to the change in the color of the dependent member which became red, at the same time painful, without attending phlegmon or inflammatory changes. The profession gave but little notice to Mitchell's original communication, but his second article published in 1878, in which fifteen cases of the disease were reported in Mitchell's graphic style, with the title "On a Rare Vasomotor Neurosis of the Extremities and on the Maladies with Which It May Be Confounded" aroused interest and since that time "Red Neuralgia" has been frequently (comparatively) diagnosticated and the complex of symptoms, because of the *erythema and pain* has been known as *erythromelalgia*.

Pathological Findings—Associated Symptoms.—The pathological findings have materially changed our original conception of this painful and obstinate affection, for it has been demonstrated by many trustworthy clinicians and pathologists that the contentions of Mitchell which separated erythromelalgia from Raynaud's disease and other organic lesions of the arteries and nervous system—which claimed that gangrenous and other necrobiotic process could never complicate the disease—have been

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upset. In considering the prognosis of erythromelalgia, its true pathologic fundament must be considered.

There are unquestionably cases of erythromelalgia in which there are no discoverable associated lesions, which correspond very closely with the original description of Mitchell. The majority of cases, however, when thoroughly investigated prove that the so-called *neuroses which affect the extremities are likely to complicate each other;* that *one may merge into the other;* that *seasonal influence materially affects the clinical history of each;* that *there may be* evidences of acroparesthesia and erythromelalgia in the *same subject at the same time;* that *these symptoms may be accompanied by evidences of the first stage of Raynaud's disease;* that *the symptoms of one of these tropho-neuroses* (?) *may disappear during a limited period to recur later, or* they may never return.

Elsner, Dehio, Sachs and Wiener, Rolleston, Sternberg, Mills, and many others have reported authentic cases of the disease in which the changes were purely vascular, of arteriosclerotic, endarteritic or endophlebitic character. Sachs holds "surely erythromelalgia is as much an arterial as a nerve disease."

My case (Elsner) was certainly a remarkable instance in which erythromelalgia and Raynaud's disease were combined. The patient at first had in 1893 numb feelings in the hands and intolerable headaches. The following winter there were the acute sufferings of erythromelalgia, burning in the palms and backs of both hands, and with the pains, the characteristic erythema. In 1896 the pains increased in the hands to an intolerable degree with hyperesthesia and profuse sweating. The redness disappeared suddenly from the thumb in September, 1896, and at the same time a red spot appeared on the right tragus, which became asphyxiated and gangrenous. A second gangrenous patch appeared over the middle of the left sternocleidomastoid muscle. Soon there was gangrene of the thumb with gradual separation of the phalanx, and final recovery.

Some cases of erythromelalgia which have persisted during long periods—twenty years and longer—have failed to show microscopic changes in the nerve structures of the painful parts; all of my cases, which I have elsewhere reported, which were examined microscopically gave evidence of "thickening of the intima of both the large and small arteries. About the small arteries were occasional foci of infiltration with lymphoid cells."

I have considered the association of vascular changes with erythromelalgia to impress upon the clinician the possibility of destructive processes with chronic cases of red neuralgia, the possibility of Raynaud's process or localized gangrene. My material justifies the conclusion that in occasional cases red neuralgia may be limited to an extremity—one or more toes or fingers—in which gangrene, deep or superficial, may develop with final relief of the pain. In all of these cases the symptomatology of

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red neuralgia is so characteristic as to make differentiation impossible if that is not the correct diagnosis. The prognosis of these conditions in which destructive processes are finally associated with erythromelalgia is further strengthened by the facts which Thoma has established in his epoch-producing work which proves that compensatory changes take place in the arteries which have remained distended for a considerable time, and which in truth are too large for the blood which courses through them.

It is a question whether erythromelalgia deserves to be dignified as a disease *per se*. In framing prognosis let the reader consider the fact that besides the conditions to which I have already referred, it may be associated with ascending degeneration of the posterior columns of the cord (Schenck), with myelitis (Woodnut), indiscriminate lesions of the cord (Collier), degenerative changes in the posterior nerve roots of the lumbar and sacral nerves without degeneration of the cord substance (Auerbach). (The only post mortem of a case of erythromelalgia on record). In my cases the material was obtained from amputated or sloughing fingers or toes and the nerves and arteries of tissue left behind.

Erythromelalgia is always a chronic process. As a rule it is progressive; in occasional cases there are periods of improvement, but rarely complete relief. Usually the pain, redness, and localized sweating are uninfluenced by treatment reaching a climax finally, and in uncomplicated cases remain unchanged during months and years (Senator, Gerhardt, Heiman, Nieden). Eulenberg reports a case which continued 23 years; the patient was 54 years of age. When 22 years of age formication and pain commenced, persisting 10 years, to be followed by the continuous symptoms of the fully developed complex.

Auerbach's case continued 20 years—finally developed tabes dorsalis with limitations of the lesion in the lumbar and sacral roots. In all cases death is due to some complication and not to erythromelalgia. Cassirer reports 5 deaths: hemiplegia in 2 (Henoch and Graves), in one dementia paralytica (Machol), one case reported by Weir Mitchell in which there was no autopsy, and one by Auerbach, above cited, in which there was tabes dorsalis with the limitation of the lesions in the lumbar and sacral roots.

Course of the Disease.—The disease may halt and remain stationary at the point reached; in rare cases there may be retrogression. I have seen one such case with final complete relief. Improvement may take place after years of suffering from this most obstinate disease, which includes a persistence of acute suffering almost unequalled by any other peripheral pain to which man is subjected.

In the average case complete dissipation of all pain and the associated manifestations—trophic and sensory—rarely follow. A dubious prognosis is safest; to offer some encouragement is justified because of improvement during considerable periods following rest of the painful part; in occa-

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sional cases the complex cures itself or yields to radical surgical treatment when gangrene follows (Elsner).

Life is not endangered though resistance is unquestionably lowered. Morphinism is likely to be the fate of many. When the complex is an expression of organic—cerebral, spinal, or vascular lesions—prognosis must be framed in accordance with the more prominent disease.

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2. Raynaud's Disease

(*Symmetrical Gangrene, Angiospastic Gangrene*)

Characteristic Symptoms.—In 1862 Raynaud described a variety of symmetrical dry gangrene "affecting the extremities, which cannot be accounted for by vascular obstruction; a variety characterized by a remarkable tendency to symmetry, affecting always similar parts of the upper or lower limbs, all four at once, in certain cases the nose and ears, and I shall try to show that this form of gangrene has its origin in a disturbance of the innervation of the capillary vessels."

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In 6,300 cases of internal disease I number 6 of Raynaud's process. Of 23,000 medical cases at Johns Hopkins Hospital in 20 years, Osler reports 19 cases, Cassirer in his classic monograph reports 168 cases collected from medical literature, and Monro reports 180 cases and estimates "that about one case occurs in 3,000 patients."

Influencing Factors.—*Sex Influence.*—Monro reports 62.5 per cent women and 37.5 per cent among men.

Age.—The disease in my experience is rarely met early in life, though Cassirer reports 22 cases under 5 years of age.

5-10	years	of	age	8	cases
11-20	"	"	"	25	"
21-30	"	"	"	40	"
31-40	"	"	"	27	"
41-50	"	"	"	28	"
Above 60	"	"	"	18	"

Family Predisposition.—It occasionally happens that family predisposition is present as has been noted in the cases of Colman and Taylor, Makins and Braman. The latter found three brothers afflicted.

Seasonal Influences.—In chronic and mild forms, during *the state of cyanosis, seasonal influences* materially affect the symptoms—one case now under observation is entirely without symptoms during the summer months but with the approach of winter, she has a combination of *acroparesthesia* with "marble fingers" and hand, alternating with "beefsteak" hand. Medicines are without influence in this case; now in its fourth year, heat and protection against cold seem to control the symptoms best. Thus far there has been no necrotic loss.

Syphilis, etc., Not Factors.—We exclude symmetrical gangrene due to syphilitic arteritis—it is not true Raynaud's disease. It offers a good prognosis, however. Monro in his monograph includes syphilis as a factor in a small proportion of cases—2.8 per cent.

Symmetrical and asymmetrical gangrene secondary to arteriosclerosis, diabetic endarteritis, nephritis and perforating ulcer of tabes are never to be included in the list of Raynaud's disease.

The stages of the progressive type of the disease may be divided into:

First stage—Local syncope
Second stage—Local asphyxia or cyanosis
Third stage—Symmetrical gangrene (dry gangrene).

First Stage—Local Syncope

For several years in mild cases (formes frustes) the extremities involved may give symptoms only on exposure during cold weather, occasionally during extreme hot weather in other cases, during which there is characteristic change of color, throbbing, aching, formication and symp-

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toms resembling acroparesthesia very closely. Such cases improve very often, but return should be prophesied in the majority.

Girls at puberty and after occasionally present with the *"beefsteak" hand.* Progression may never follow, but persistence of discomfort and vasomotor symptoms are likely to persist. In occasional cases there is, during the first stage, some *evidence of the disease in the cheeks or in one or both ears.* In one of my cases there was a limited *necrobiosis* (superficial) of one tragus with subsequent improvement of the hands, so far as subjective symptoms were concerned, but the fingers were more or less stiff as the result of a *sclerodermic thickening* which followed.

In most of the mild cases there is no marked cyanosis; when present it is of short duration, insufficient to cause destructive change. In some cases with freedom from care, emotion, or exposure, the fresh attacks of syncope may be prevented or postponed.

Cases in which the mild form or early stage is limited to one toe or finger may never progress beyond this stage or extend to other parts. I have noted a few cases in which, after there has been local syncope during a number of years, there have been *characteristic pinhead or split-pea sized, cup-shaped losses of epithelium from the toes or fingers with subsequent scleroderma and some change in the shape of the digits beyond which the disease has not extended,* and such patients were but little inconvenienced, lived many years, and died of intercurrent disease.

Patients may go on with "dead fingers"—numb and analgesic—during varying periods (hours, days, or months) with final relief, or the condition may remain, or there may be progression to gangrene.

Second Stage—Local Asphyxia or Cyanosis

During this stage in accordance with the severity of the disease the extremities involved are cold and cyanotic. Severe and rapidly advancing cases may escape the first stage entirely and at once present marked evidences of cyanosis. Deep blue and black discoloration of the nails with corresponding changes in the skin argue in favor of a severe process, and such cases usually advance with considerable rapidity to the third stage, or gangrene. There may be periods of improvement after the second stage is fully established even in cases which at times appear threatening to the parts involved. In some of these the advance to but limited loss of tissue (epithelial or superficial) may end the gangrenous feature of the disease. Not all members will be equally involved in average cases, for one finger may show marked asphyxia while its neighbor may remain in syncope. In some of these cases *active hyperemia* may persist during long periods; in other cases the sequence of syncope and asphyxia of a member may be exceedingly and surprising short.

As a rule, in an acute exacerbation, there is first the *"marble hand"*

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or finger, in which the part is anemic (white), then follows active hyperemia in which the color is deep—usually blue—and finally a longer period of red. *Repeated or long continued active hyperemia with final asphyxia* may lead to *necrosis* or *gangrene.* In the severe cases *involvement of the nose and ear,* one or both at times, may be present and losses of tissue, either deep or superficial follow.

When asphyxia persists and the livid part is pricked and only dark blood escapes, gangrene may soon be expected to follow. Monro says: "The duration of the attack varies from a few minutes to hours or even days. Several attacks may occur in one day, or one in several days or weeks, or the intervals may be much longer." Some cases show "a high degree of paroxysm, while others which persist with but little change for prolonged periods can justly be ascribed as chronic."

The *general condition* of these patients remains uninfluenced in most cases during this and the first stage, save as the sensory disturbances depress, rob them of sleep and appetite. *Recurrence of local asphyxia* may continue during many years without marked advance of trophic change. Young children have been reported as permanently relieved after a prolonged series of repeated exacerbations of local asphyxia. In one of these cases (Johnston) the "local asphyxia came to an end suddenly and permanently after two months." Monro feels justified in holding "an attack of Raynaud's disease may be constituted simply by one attack of local asphyxia prolonged over months without interruption.

Third Stage. Symmetrical Gangrene

Monro, whom we frequently quote because he is unquestionably the ablest authority on the subject, says: "While local syncope is met with in 50 per cent, and local asphyxia in 94 per cent, necrosis of tissue, either slight or serious, occurs in 68 per cent of Raynaud's disease."

Years may lapse before the first or second stages are followed by gangrene. Occasional cases may develop gangrene without preceding circulatory symptoms or trophic changes of any preceding stage. The loss of tissue or a member (usually toe or finger tip) is in most cases followed by prompt repair, but with more or less trophic changes. The deep gangrenous changes may leave surfaces which require several months to heal; often the reparative process is exceedingly slow. Church and Peterson report deaths in infants a few days after the beginning of symptoms, and occasionally from uremia in aged patients. Such termination I have not experienced in uncomplicated cases.

Complications

The *acute infections* (typhus, typhoid, smallpox, scarlet fever, diphtheria, measles, pertussis, erysipelas, influenza, syphilis, tuberculosis, ma-

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laria, rheumatism, rheumatoid arthritis, quinsy, splenic enlargement, hemorrhagic and suppurative processes) have in rare instances been followed by Raynaud's disease (Monro).

I have seen two deaths from *tuberculosis* follow Raynaud's disease. The relatively high mortality from tuberculosis of Raynaud patients has been noted by many clinicians, but there are no positive evidences, because of the general prevalence and frequency of tuberculosis, that Raynaud's disease bears more than an accidental relation to the former.

Rheumatism unquestionably bears a close relation to the disease for it is found to have preceded it in a large number of cases.

Psychic disturbances were present in 4½ per cent of Monro's cases.

Scleroderma already mentioned is frequent. This is usually associated with the multiple cup-shaped and limited losses of tissue mentioned in the preceding pages or follows more extensive gangrene.

Basedow's disease with mitral lesions has been found in occasional cases (Tompson, Bret and Chalier).

Osborne makes the positive statement that "Raynaud's disease is not a distinct entity . . . the disturbance of one or more internal secreting glands . . . there is always apparently some disturbance of the thyroid gland, perhaps a diminution of the vasodilator stuff of this gland."

Osborne further claims that the prognosis of the syndrome is improved in the majority of cases, perhaps all, by the thyroid treatment and that it "cures some cases."

The association of *erythromelalgia with asphyxia and gangrene* has been separately considered (See Erythromelalgia). In these cases the terminal stage of Raynaud's process may be followed by the relief of all sensory symptoms, and barring the deformity and stiffness resulting, there is no further suffering.

Kidney, cerebral, and *ocular symptoms* may influence prognosis unfavorably; such complications are infrequent.

Albuminuria may be transitory without influence on the process, though it is probably due to vascular anomalies of a fleeting character.

Repeated paroxysmal hemoglobinuria may finally cease entirely, or in occasional cases nephritis may finally develop.

The eye symptoms—*temporary amblyopia*—probably due to vascular spasm, are not lasting.

In occasional cases moderate *paresis* of one extremity or *hemiplegia* may come and go without leaving permanent damage. The same is true of *aphasia* which may in the occasional cases of transitory hemiplegia alarm the patient who may ultimately recover.

Osler and Thomas report a most interesting and unique case in which "the wide symptomatology of the disease" was illustrated. The patient was 23 years of age, "had typical Raynaud's disease—fingers, toes, ears, nose—and cyanosis often preceded superficial necrosis. The attacks oc

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curred in the winter; in warm weather he was perfectly well. *Epileptic attacks accompanied the outbreaks* of local cyanosis, but only in the winter, when he also had hemoglobinuria." The case was followed for over three years, the cyanosis persisted but necrosis was "never widespread." After three years "the epilepsy ceased but the winter attacks came on as usual and were associated with crises of abdominal pain, just like those of angioneurotic edema, and he had swelling of the spleen." I quote this case fully because it shows the protean character of the disease and complicating conditions, and the prognostic problems associated are fully accented by it.

I have never in practice had a death directly traceable to the disease, neither has it seemed to shorten life when uncomplicated. Great caution is necessary in the prognosis of individual cases for it is impossible to foretell the course of even advanced cases, much less the incipient. The majority of my cases, in which complications did not interfere, lived to fall into long periods of comparative relief after the separation of the gangrenous tissue; in some there were exacerbations during the winter months, in a small proportion change of work and scene or removal to an equable and warm climate had a wholesome effect.

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3. Acroparesthesia

In 1890 Fr. Schultz described a condition in which it may be assumed that there is more or less *vasoconstriction of the hands* associated with *paresthesia*—tingling, numbness, clumsiness, "velvety feeling," creeping crawling sensations—at times burning, with pain in some cases. It is usually found in women (washerwomen)—those whose hands are in water while at work. In the United States it is relatively frequent, as are most

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trophoneuroses of the extremities among Jewish patients in dispensary practice.

There are unquestionably cases in which with positive evidences of acroparesthesia there are suggestive appearances of syncope and asphyxia; in fact the relations of the various trophoneuroses which affect the extremities are so close as to lead to the conclusion that, as I have suggested in the study of erythromelalgia and Raynaud's disease, these various complexes may exist together or one may follow the other.

Acroparesthesia is most likely to develop upon a fundament of *heredity,* upon a *psychoneurotic basis,* often in the presence of *hysteria* or *neurasthenia.* When the disease develops in men, these stigmata are particularly prominent and it is not at all unusual to find complications which may include organic disease of the nervous system or of the ductless glands. One of my cases which persisted during many years—most of which time the man traveled carrying heavy satchels (to which fact he attributed his sensory disturbances) suddenly developed an atypical type of *hyperthyroidea.* The development of the disease is usually symmetrical, but there are exceptions to this behavior.

Acute and frequently repeated exacerbations may be prophesied with considerable certainty. In some cases symptoms (paresthesia) may be continuous, and these may merge into the milder forms of Raynaud's disease. *Excessive sweating* may be the end of a period of acute symptoms. *Migraine* and *gastric disturbances* may persist during acute *exacerbations. Acroparesthesia per se does not lead to asphyxia or gangrene*—neither will the muscles of the affected parts atrophy, though there may be transitory weakness as shown by the dynamometer.

In women who are obliged to support themselves, usually by washing, it has seemed that removal from damp homes, the proper ventilation of bed and workrooms, the relief of uterine anomalies, the menopause, change of scene with rest and psychic influences, have had a wholesome effect—with the correction of gastro-intestinal disturbances which are present in most cases.

The complex per se is not of serious import; is likely to prove chronic, and while a slight remnant of paresthesia usually remains, it is not sufficient to prove a serious or annoying handicap.

4. Angioneurotic Edema

(*Giant Urticaria, Acute Circumscribed Edema, Quincke's Disease* (1882), *Periodic Swelling*)

Milton in 1876 described a condition of "giant urticaria" which was finally fully considered in Quincke's description of *edema circumscriptum cutis* in 1882, to which the name of Quincke's disease has been given. The symptoms develop suddenly and consist of edema of the face, as a

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rule, with corresponding deforming enlargement of the parts involved, which continues during several hours—rarely a day or two—usually associated with more or less gastro-intestinal disturbance, foul breath, at times threatening edema of the larynx, with or without swelling of the tongue. The edema may be associated with itching and in most cases abnormal "fullness." In most cases recurrences may be prognosticated.

It is exceedingly difficult in the individual case to determine the underlying cause of these oft-repeated edemas. The interval between the attacks is variable; in some cases several years may elapse, in others there seems to be a cycle of evanescent edemas usually swelling parts of the face at a time, or the genitalia, or there may be alternation with gastro-intestinal crises. Roger Morris believes that he has demonstrated from the bits of mucosa in the wash water taken from the stomach, positive evidences of edema. Single attacks average from six to eight hours. They are not painful or threatening save as they cause *respiratory obstruction* due to *edema of the glottis.* This may in occasional cases involve but one-half of the glottis—a condition which I found alarming and demanded immediate free incision to prevent increasing air hunger.

Pulmonary edema and edema of the glottis are the leading life-threatening features of Quincke's disease; without these the disease is not serious, but exceedingly annoying. Most of my cases have cured themselves after several years (2 to 10) of recurring symptoms. The individual case offers encouragement for prognosis in proportion to the ability of the clinician to unearth the cause; usually this is impossible. The cases burdened with a striking *heredity* (Quincke, Osler), purpuric conditions, recurring erythema with visceral complications and nephritis or cyclic albuminuria may prove serious—more because of the associated lesions than from the giant urticaria. With the disappearance of the annoying edema, the patient usually returns to perfect health and in some cases life is "of exceptional duration." Young subjects offer a favorable prognosis. There are unquestionably cases of gastro-intestinal edema which give rise to visceral symptoms resembling acute infections (appendicitis, enteritis, intestinal obstruction) which require accurate differentiation, that incorrect diagnosis and prognosis may not lead to radical (surgical) measures (See also Serous Meningitis).

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5. *Scleroderma*

Thirial in 1845 described a peculiar nutritional skin lesion, either circumscribed (morphea) or diffuse, in which there is a leathery thickening or induration of the skin which is tightly stretched over and adherent to the underlying subcutaneous tissue. The *disease is progressive, atrophic, and may involve the subcutaneous connective tissue, the muscles, and the bone tissue under the changed skin.*

Heredity plays only an unimportant role in the pathogenesis of this unique condition. The true cause is unknown though cases have been traced to a variety of causes, including the acute infections (typhoid, erysipelas, influenza, syphilis, tuberculosis and smallpox), exposure to heat and cold, to wet, pregnancy, trauma, psychic factors—as sudden shock, emotion and long continued worry. I have found in most of my cases which developed late in life, organic disease of the heart and vascular system. I also refer to *localized scleroderma* as it follows or is associated with acroparesthesia, erythromelalgia and Raynaud's disease (See separate chapters).

Typical cases progress slowly, and as a rule symmetrically. There are acute cases, but these are exceedingly rare.

Pigment deposit and bronzing are late developments, when the skin is so tightly drawn over the underlying tissue as to prevent folding. When the face is involved and the disease progresses, the skin is tightly drawn and in the end the expression is characteristic.

Recession of lesions is not to be expected though the changes may halt in any stage of the disease. *Atrophy is the fate of the involved skin and tissues.*

"Sclerodactylie" is the term used by the Germans to characterize the changes of a sclerodermic character associated with Raynaud's disease and tissue loss (gangrene) (See Raynaud's Disease).

Circumscribed scleroderma (morphea) involves only limited stripes or areas of skin, without far reaching damage.

Joint changes may be expected in some cases with some contraction, as a rule; these do not materially interfere with the activity of the patient. *When scleroderma is a complication of Graves' disease or Addison's complex,* the prognosis of the more serious disease decides the fate of the patient.

General Observations.—To recapitulate from the foregoing statements: Scleroderma is a chronic progressive disease which remains uninfluenced by treatment, which may remain circumscribed to a limited area or may be diffuse. It does not destroy life and it may remain stationary after months or years of progression. *Acute cases* (Heynacher) have been observed in which cure followed. It is not uncommon to find cases which have persisted as long as thirty and forty years. Involvement of

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the face and fixation of the jaw may cause nutritional disturbances—marasmus—and consecutive asthenia. Children (Tomaczewski) offer a favorable prognosis in individual cases. Once advanced to the stage of atrophy there is no hope of restitution. In infants acute diffuse scleroderma may be associated with general infection which may lead to death, as was proved by Barker's case in which the sclerodermic child, aged two and a half months, died of pleuropneumonia and general streptococcus infection.

The majority of sclerodermics die of intercurrent disease. The influence of thyroid feeding has encouraged some dermatologists and neurologists to offer a better prognosis than has been previously given. My experience with a limited material and thyroid therapy does not justify any conclusions of value at the present time.

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6. Adiposis dolorosa

(Dercum's Disease)

Dercum, in 1888, called attention to a condition found in male adults oftener than in women, with fat deposits which are painful or sensitive, in which there may be marked weakness, some genito-urinary disturbance, and mental anomalies. The fat deposits may be either nodular, circumscribed, or diffuse. The disease, in the light of our increased knowledge of the functions of the pituitary body, should be considered to be due to hypopituitarism. Indeed tumor of the pituitary (Dercum and McCarthy) has been found to present the characteristic clinical picture of adiposis dolorosa with "hypoplasia of the genital organs, extensive infiltration of the fat and hemolymph glands."

Price's observations in eight autopsies confirm the conclusions concerning these painful fat deposits to which pathologists are fast subscribing, which attribute the symptoms to organic change in the pituitary gland. Pain is the leading feature and is persistent, and with the general weakness remains uninfluenced by treatment.

The *psychic symptoms* may remain unchanged or may advance to full *mental alienation.* The disease does not lead to death, but unless based on the theory of hypopituitarism, and unless surgical intervention or pituitary therapy brings relief (at present sub judice), we shall be forced to give a doleful prognosis so far as the relief of symptoms is concerned.

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7. *Intermittent Dropsy of the Joints*

(*Angioneural Arthrosis*—Solis-Cohen)

Perrin in 1845, Moore in 1852 and 1868, Friedenberg in 1888, and Schlesinger in 1900, called attention to a class of cases in which there is paroxysmal return (intermittent) of dropsy of one or more joints. Cohen includes the intermittent dropsy of joints (not dependent upon infection) among the "angioneural arthroses." He says "the term 'hydrops articulorum periodica' or 'hydrops articulorum intermittens' has been applied to the one variety of vasomotor joint disorder that has thus far been definitely recognized; but it is applicable to that variety alone." It is a question whether these suddenly recurring effusions into the joint are not atypical types of angioneurotic edema (Quincke's disease). The knee joint is usually dropsical, though in some, both knee joints are suddenly involved; other joints may swell, and occasionally there is invasion of the jaw and separate parts of the spinal column.

Schlesinger has reported intermittent dropsies of the tendon sheaths and Cassirer painful edemas of the muscles. Cohen's characterization of these cases as *'vasomotor ataxia'* is a happy and suggestive one. Once the disease is established, recurrence should be expected at intervals which average between seven to fourteen days. Three months have elapsed without return in reported cases. In a few cases there is great regularity in the time of recurrence. Periods of four weeks may be considered long. Oppenheim reports recurrence and disappearance during intervals of a few minutes. There are patients in whom there is such marked periodicity as to make it possible to foretell the day of return of the joint dropsy. One of my cases during many years developed dropsy of the right hip with each menstrual period, entirely uninfluenced by rest or treatment. I have seen but three cases in private and hospital practice, in all of which there were no marked pains; in none was there fever nor constitutional disturbances. The *duration of the swelling* is not always the same. It may continue but a few hours, a single day, or in the average case, from two to seven or eight days.

My cases were not dependent upon discoverable causes. His reports *gouty conditions* complicating the complex, while Oppenheim has found it

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with *Basedow's disease,* and angina pectoris. Schlesinger and others prove that the association with functional and organic disease is not uncommon. *Differentiation of polyarthritic conditions, gout,* and other *afebrile arthritic lesions* is not difficult. Cohen believes that the process may be influenced and attacks postponed by treatment. It is questionable whether the cases reported as cured (Wiesinger) by surgical interference (aspiration and iodin injection) were true 'angioneural arthrosis.' The prognosis so far as control of the symptoms is concerned is not good; the process is exceedingly rebellious and chronic. *Psychic influences* (suggestion) have seemed to exert some control over the disease in subjects with a marked hysterical or neurasthenic habit.

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8. Persistent Hereditary Edema of the Legs

(Milroy's Disease, Hereditary Tropho-edema)

I have had no experience with hereditary edema in my practice. Milroy, in 1893, was the first to describe persistent and hereditary edema of the legs which gave the disease its name—Milroy's disease.

Henry Meigs (1899) reported a family in which eight members were affected, both men and women, through four generations. All of these cases were without known cause and without general disturbance. Osler says: "It is a fairly common complaint affecting males and females equally."

In six generations among 97 in Milroy's series, 22 presented with characteristic symptoms. Hope and French found in their series 13 to 42 persons in five generations. All of these cases presented the same features: painless edema of the legs which persisted, usually appearing about puberty. In some cases there were febrile disturbances following chills and acute exacerbations in swellings. The condition does not influence the general health of those chosen, causes but little discomfort; it has not been known to shorten life, but refuses to yield to any known treatment.

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Diseases of the Sympathetic Nervous System

Much light has been thrown on the anatomic structure of the sympathetic system during the past few years by Eulenberg and Guttman, Gaskel, Langley, Anderson, and many others. Our knowledge of the influence of the sympathetic on constitutional and visceral disease, while materially enlarged thereby is still exceedingly limited.

The sympathetic system innervates the nonstriated muscles of the body, the blood vessels, the intestines, the heart and glands, and delivers impulses to the central nervous system from the viscera.

From the anatomic structure and the distribution of the sympathetic nerve, we recognize its influence in many diseases of the vital organs. It cannot be considered alone in the prognosis of these innumerable conditions.

9. Paralysis of the Cervical Sympathetic

Causes.—Paralysis of the cervical sympathetic may follow a lesion anywhere in its course. The leading causes are *myelitis, traumatism,* leading to *injury of the upper dorsal segments of the cord, vertebral caries, of tuberculous origin, metastases or tumors* (*aneurism*) *causing pressure.*

Birth palsies have occasionally included the cervical sympathetic.

Congenital and hereditary paralyses of the cervical sympathetic have also been reported.

Symptoms.—The symptoms of cervical sympathetic paralysis are contracted pupil (myosis) on the side of the lesion, narrowed palpebral fissure, sunken eye, anomalies of sweat secretion on the same side of the face, and often paralysis of the Klumpke type (lower brachial).

Facial hemiatrophy and the premature change of the hair to gray on the side of the lesion has also been noted.

There is a superior sympathetic center in the *medulla oblongata* which accounts for symptoms of sympathetic paralysis in some cases of disease of the medulla. Besides the symptoms of sympathetic paralysis above noted, there is weakness of the limbs of the opposite side, tendency to fall toward the side of the lesion, *vertigo, nystagmus* and *involvement of the muscles of phonation, articulation and deglutition.*

Prognosis.—In none of the conditions in which an organic lesion has

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caused cervical sympathetic paralysis does treatment exert the slightest influence.

The symptoms referable to disturbance of the *visceral sympathetic system* are vague and uncertain.

Various symptoms have been charged to sympathetic disturbance but the entire symptomatology is still in the realm of speculation and positive conclusions are not justified. Whether the sympathetic is the cause of *gastric crises and other visceral and distant symptoms of tabes,* is also problematic.

The influence of the sympathetic in exophthalmic goiter and suprarenal disease has been differently interpreted and is also unsettled (See separate consideration of both diseases).

10. Irritation of the Cervical Sympathetic

Irritation of the cervical sympathetic causes the following symptoms which are the opposite of paralysis, and include *mydriasis* (dilated pupil), *widened palpebral fissure, prominent eyeball, and delay in the lowering of the eyeball* (Graeffe symptom).

(For a full consideration of the influence of the sympathetic system on symptomatology without positive conclusions but with abundant references to recent work, the reader is referred to Holmes' article in Volume VII, Allbutt and Rolleston's System of Medicine, second edition, pages 492-500.)

11. Vagotonia

Included in the functional disturbances attributed to altered function or a changed reciprocal relation of the sympathetic system and the pneumogastric nerve, Eppinger and Hess have called attention to the fact that there are individuals who react abnormally to drugs which influence the vagus or the sympathetic, and they speak of these as vagotropic and sympathicotropic, respectively.

Normally *pilocarpin* (0.01 gm., 1/6 grain) produces hyperidrosis, salivation, hyperacidity, eosinophilia, slows the pulse, and causes spastic constipation.

Atropin paralyzes the pneumogastric, hence has the opposite effect of pilocarpin, causing rapid pulse and pupillary changes with dryness, etc. There is a reciprocal relation which continues the normal balance or tone.

With the vagotropic disposition there is a powerful idiosyncrasy, *oversensitiveness to pilocarpin,* and the symptom complex of vagotonia, which is a true neurosis and is associated with a marked neurasthenic predisposition results. The symptoms of vagotonia are contracted pupil, bradycardia, asthma, laryngeal spasm, gastrosuccorrhea, pyloric spasm, vagotonic conditions of the stomach shown by x-ray examination, mucous

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colitis, and obstinate constipation; all of these symptoms are favorably influenced by atropin, and these patients show a high tolerance for adrenalin and the carbohydrates.

In all of these cases before giving a favorable prognosis, so far as life is concerned a cautious differentiation is necessary, as paroxysmal bradycardia and some of the associated symptoms may be caused by organic lesions—among these, Stokes-Adams disease and myocardial degeneration, arteriosclerosis, and cerebral lesions.

Life may not be materially shortened by uncomplicated vagotonia, but it is a condition which is likely to be chronic and recurrent. Most of my cases in which I originally made the diagnosis were finally found to be of organic origin, due to one of the above mentioned conditions.

12. *Sympathicotonia*

Sympathicotonia is associated with the opposite symptoms, i. e., tachycardia, adrenalin glycosuria, and adrenalin mydriasis. In these cases pilocarpin is without effect and fails to produce the physiologic symptoms above mentioned.

The entire subject of vagotonia and the opposite condition, sympathicotonia are under consideration by the profession, and while there is much which tends to prove the contentions of Eppinger and Hess that there are vagotropic and sympathicotropic individuals, positive anatomic lesions must always, as already suggested, lead to the thorough consideration of the suggestive symptoms and great caution must be used in determining the tolerance of the patient to the drugs—particularly adrenalin—which may, in large doses, lead to pulmonary edema and emboli in the liver and mesentery.

Bergman and Curschmann have also called attention to the dangers associated with the use of adrenalin in large doses.

The prognostic significance of the many other conditions referable to the sympathetic nervous system are considered in connection with neurasthenia, hysteria and the trophoneuroses to which the reader is referred.

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Section VIII

Diseases of the Locomotor System

A. Diseases of the Muscles

1. Myalgia—Myositis

(*Muscular Rheumatism*)

Causes.—Myalgia, or muscular pain, is probably due to a mild form of myositis in most cases. *There are individuals who are predisposed to myalgia* on slight cause, in whom it may be safely assumed that there is some *metabolic fault or toxemia. Trauma, exposure to cold, syphilis, and acute infections* are among the causes of myalgia.

The Myalgias.—The *occupational myalgias* are also of myositic origin (piano and violin players, shovelers, molders, and a score of other occupations).

Lumbar myalgia or lumbago is frequent in those predisposed, as is also the cervical variety. In some lumbar and pectoral myalgias, *anemia* is a pathogenic factor, and in women, there are *reflex pains in the muscles of the body* which are due to *menstrual anomalies or diseases of the generative organs.*

Prognosis of the Myalgias.—The prognosis of the myalgias is good. The disease yields to rest and local treatment in from two to four days in most cases. *Recurrence* is the rule. The cause naturally influences the prognosis.

In *gouty, diabetic,* and so-called *rheumatic patients,* also with *arteriosclerosis,* there are those in whom some muscles are almost always tender and in whom the movement of these is exceedingly painful. There are also patients in whom parts of a muscle are found tender on deep pressure (*"Muskelschwiele"*) which massage relieves temporarily. These cases are only cured or relieved when the underlying fault is unearthed and removed.

Myositis.—*True myositis* is not a frequent disease; it may be *localized or general. With the infections there are often symptoms of poly-*

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myositis. Among the diseases in which muscle pains are severe are *trichinosis, smallpox, Asiatic cholera, also influenza.*

Dermatomyositis and *neuromyositis* are rare. In the former the myositis is *multiple* and there is more or less *dermatitis* and *edema, fever and constitutional disturbances and absence of reflexes;* in the latter there is a mixture of neuritis and myositis. When there are complicated serious diseases—such as tuberculosis—the prognosis is grave. In the idiopathic *dermatomyositis* the prognosis may be ominous, though most cases recover. The mortality is 20 per cent.

When the heart muscle (*myocarditis hemorrhagica*) is involved the prognosis is correspondingly bad.

When the disease is without known cause, *trichinosis* should always be suspected. *Neuromyositis* may at times prove to be a forerunner of progressive muscular atrophy.

Gummata of the muscles yield to treatment (See Syphilis).

Abscess of the muscle offers a good prognosis unless multiple and dependent on malignant infection.

2. *Progressive Myositis ossificans*

Myositis ossificans is a rare disease in which there are periods of more or less fever and evidences of local muscular inflammation followed by the deposit of bone tissue in the muscle. There are repeated exacerbations —almost always *febrile,* always associated with evidences of *fresh myositis,* which in turn are followed by *fresh deposit of bone.* The disease usually begins in the back and neck muscles. When progressive—the usual tendency—uninfluenced by treatment, it may involve most of the voluntary muscles of the body, causing malformations and limiting the usefulness of the patient.

The symptoms of the acute exacerbations may persist several days or weeks.

3. *Thomsen's Disease*

(*Myotonia*)

Thomsen's disease is a *primary myopathy in which voluntary movement is checked by a spasm of the muscles.*

The disease was first described by Thomsen, in whose family it has continued during four generations, and includes over twenty cases.

There are occasional cases not hereditary; in some of these the symptoms disappear without being reproduced in the offspring. Male children are oftener afflicted than female; the symptoms begin during the first years of life.

The muscular development is good; at times there is *overdevelopment* but there is almost always *muscular weakness.*

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The spasm—rigidity of the muscle on voluntary movement—always remains *the* characteristic of the disease and this continues during several seconds.

The reflexes are not changed, neither are there sensory symptoms.

The *myotonic reaction of Erb* is present in which the muscular contractions caused by either the faradic or galvanic current are abnormally slow and relax gradually, while the wavelike contractions pass from the negative to the positive pole. Weak faradic current causes tonic contraction which continues abnormally long. There is no reaction of degeneration. The spasm is increased by excitement or hurry.

The disease does not shorten life; it remains uninfluenced by treatment and shows no tendency to progress. As the children grow, they learn to accommodate themselves to the spasm; occasionally there are periods *of remission.*

In some cases there are psychic disturbances, epilepsy, migraine, and congenital anomalies, which are persistent. No treatment influences these complications materially.

4. Paramyoclonus multiplex

(*Myoclonia*)

Friedreich, in 1881, first called attention to this disease in which there may be *continuous or paroxysmal contractions of the muscles of the extremities—usually in males. The contractions are usually short and clonic with fibrillary tremor following in some cases.* They are *symmetrical without changed electric reaction,* and *are increased by emotion, fright and exhaustion. Exercise tends to decrease the spasm.*

The *reflexes* are slightly exalted. There are no associated symptoms referable to the nervous system.

Only rarely are the contractions tonic or severe; when they are, the differentiation of the disease from epilepsy will be necessary and easy, as the spasm may be sufficiently severe to throw the patient.

Myoclonus seems to be a *family disease,* particularly those forms which are *epileptoid* in character, which Unverricht described, also Jacobsohn.

The spasms cease during sleep and are uninfluenced by treatment. The disease is without effect on the general health of the patient.

5. Akinesia algera

Moebius described a complex which is characterized by such extreme pain as to lead to unwillingness of the patient to move the muscles of the body; it leads to chronic invalidism during which the patients are bedridden much of the time.

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There is no known pathologic cause.

The patients are usually *neurasthenic, hysterical* individuals, often depressed and hypochondriacal. In a case recently seen there were no movements of any muscles, including deglutition, which the patient did not fear to make because of the pain. The pains continue for several minutes after the muscles are used. These patients hesitate long before attempting to move or act. There is no paralysis.

Moebius and Erb relegate the pains to the *psychalgias.*

Whatever the cause or pathology, the complex is associated with great suffering, including mental pang; the patients are practically helpless when in the advanced stage—because no attempt is made to move any part of the body and only the necessary acts are performed to maintain life, and for these repeated suggestion and encouragement are required. The eye muscles are involved in the psychalgia which leads the patient to lie with the eyes closed most of the time. One of my cases developed photophobia with intense pain and emaciation because of the dysphagia and her fear of taking food.

My material includes two cases: one has been bedridden over twenty years, without the slightest improvement, extremely emaciated, taking only sufficient food to sustain her; the second case has advanced in six years so that there is fear of all movement, tachycardia, and psychasthenia. With increase of symptoms and advance of the hypersensitive condition of the muscles, the fear of impending death has in the second case been among the most annoying of the symptoms. In this case repeated lumbar puncture and Wassermann reactions have given no clue to a pathologic change.

Occasional cases recover under the influence of suggestion, painstaking and long continued supervision, even after advanced akinesis, but only when the patients are removed from their usual surroundings. In a number of cases death is caused either by complicating infection, other complications, or with marasmus and extreme asthenia; the end follows years of suffering. Akinesia algeria is comparatively rare, in over 6,700 indexed cases of internal disease, I found but two well pronounced examples of the complex. It is always to be considered of grave import.

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B. Diseases of the Joints

Destructive Chronic Polyarthritis

(a) Arthritis deformans

(*Rheumatoid Arthritis*)

(b) Chronic Articular Rheumatism

(a) Arthritis deformans, or chronic rheumatoid arthritis, and (b) chronic articular rheumatism are so closely allied pathologically and clinically that many consider their differentiation impossible. *"Chronic rheumatism" is a term which should be discarded, and I have therefore considered it wise to classify these kindred conditions under the head of Destructive Chronic Polyarthritis.*

The type usually known as *arthritis deformans* is a chronic progressive joint affection, in all probability at first a chronic inflammation involving the articular cartilages, periarticular tissue, ultimately changing the bone structure and the joint as a result of progressive hypertrophy with changes in the synovial membranes, all of which are associated with loss of function and deformity leading to misshapen joints and associated muscular atrophy.

Herberden, in 1804, recognized arthritis deformans as different from gout and rheumatism. No benefit can come from an attempt in the present state of our knowledge to differentiate cases of arthritis deformans in practice from those cases of so called "chronic rheumatism" because the latter is a misnomer; the conditions, as in the former, are due to infection, and while in some the lesions are limited to the fibrous structures of the joint, as the process advances slowly, arthritic changes follow which parallel true arthritis deformans. I therefore exclude "chronic rheumatism" from consideration believing that the deforming arthritides should include all such cases as are not classified under the acute or subacute infectious polyarthritides (See Infectious Diseases) and prefer their characterization as *"destructive polyarthritis."*

Etiology and Pathology.—The profession is passing through a transition period so far as the etiology and pathology of arthritis deformans are concerned. The results of recent investigations justify the conclusion that the overwhelming number of *joint conditions which have in the past been considered of "doubtful origin," known as arthritis deformans, are secondary and dependent upon a focus somewhere in the body, which in many cases can be discovered and attacked. On the other hand there are, comparatively considered, a large number of cases in which the joint symptoms are the same as in those cases in which a primary focus of infection is discoverable, in which careful search fails to give the slightest clue*

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of the cause and the disease remains uninfluenced, stationary, or the multiple invasion of joints progresses.

Causes and Sources of Infection.—For purposes of prognosis *it is safest to assume that all forms of the disease are infectious,* that the theories advanced in the past which included a close relation of the far-reaching changes with rheumatism and gout or an inherent tendency to joint changes (diathesis), faulty nutrition, tendency to characteristic degenerations, changes in the nervous system (cord), and a variety of other causes including traumatism must be surrendered (See McCrae). Naturally the prognosis of any form of arthritis is materially improved by the detection of the pathogenic focus; without such knowledge the process cannot be influenced. The work of Rosenow, Billings, and others in this field proves the great importance of correlating the bacteriologic with the clinical study of individual cases.

Let it be remembered that the focus may hold the streptococcus without giving rise to active local symptoms of disease. The *tonsils* harbor the germ in much the larger number of cases; often it is possible only by thorough enucleation to trace the infection to these, because of the surprising and almost immediate improvement which follows.

Advancing arthritis with or without febrile movement may be traced by means of x-ray pictures to the dental alveoli, in which cases there are often no other clinical evidences of anomalies. Acting upon the information gained, the prognosis in these cases becomes encouraging. In over 50 per cent there is *pyorrhea alveolaris* and carious teeth (Cambridge Report, etc.). Some of the results after the treatment of the local process have been surprisingly prompt and favorable. In one case seen while writing this chapter, a woman aged about forty-two, in which the disease was making rapid advance, the refinements of diagnosis proved alveolar and tonsillar infection which when radically removed, lead to almost immediate remission of all constitutional and joint symptoms after more than a year of progression.

Infection to the joints which becomes chronic may proceed from any of the mucous surfaces of the body, including the gall-bladder, the intestinal mucosa, the appendix, the bladder, and the prostate gland. In the aged, "morbus coxarius senilis" and occasional types of *"stiff spine"* unquestionably originate in preceding infection, in which the joint changes were insidious, finally reaching their full development as the resistance of the patient is reduced. This experience I have repeatedly confirmed in practice when, with advancing cardiovascular or nephritic changes, the joints have grown progressively worse. *Chronic myositis* often complicates arthritis and in severe cases may be general.

The prognosis is improved by the ability of some (by keeping in motion) to help themselves and to influence faulty metabolism.

Sex.—The collective investigation of the Cambridge Committee proved

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the prodominance of females over male chronic arthritis (76.5 to 23.5 per cent).

Age.—Age is no bar to the disease, though children are rarely afflicted. In the Cambridge collection one case was found in a child 18 months old.

The Cambridge cases gave the following ages when they first came under observation:

Years.	*Number.*	*Percentage.*
1-10	4	1.1
11-20	18	5.1
21-30	68	19.4
31-40	90	25.7
41-50	64	18.2
51-60	57	16.2
61-70	37	10.5
71-80	10	2.8
81-90	2	0.6

Experience proves the greater frequency of the involvement of one large joint (hip usually) in the older subjects, while the *periarticular* and *atrophic forms are more frequent in early life than is the osteitic* and *hypertrophic* disease.

Race.—McCrae has called attention to the relative immunity of the colored race, for which he has no explanation to offer.

Occupation.—The larger number of my cases show slight influence of occupation but little of *social status.* Of four cases now under treatment which represent the average, none are living under unfavorable surroundings and all have always had comfortable and sanitary homes. Unquestionably many rheumatoid arthritics have been unfavorbly influenced by indoor occupations; in men, alcoholism has seemed to prove inviting.

Marie's Disease.—With *spondylitis* (*Marie's disease*) *"spondylose rizomyelique"* traumatism is often (25 per cent) supposed to be the exciting factor (Wehrsig), but close study of these cases will prove that the condition simply required the match to kindle the fire. The frequent complication of *tuberculosis* with Marie's stiff spine is due to the lowered resistance of these patients and their inability to take advantage of favorable conditions.

Marie's disease advances to complete stiffness of the spine; it is not infrequent, considering the entire number of typical forms of arthritis deformans. My material includes 7 cases of stiff spine in 6,300 of internal diseases and 49 of the typical forms of rheumatoid arthritis. The *radiograph* in the advanced cases shows positive and characteristic changes. Chronic cases will not be relieved by treatment. This is particularly true of the disease after middle life. Associated with multiple joint changes and not far advanced in young subjects in whom a focus of infection is discovered and removed, the prognosis is relatively good. In a number

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of cases the changes limited to the spine alone progress to stiffness, limit motion, but do not advance. Such patients learn to accommodate themselves to the handicap. The *early detection* of the disease in young and active subjects, in whom the coöperation of the patient can be thoroughly enlisted, adds to the chances of controlling the process. Those with a strong will, who persist in the use of the affected parts in spite of acute pain, who are in a position to nourish themselves well and attend to metabolic faults, often control the disease satisfactorily. Naturally, as has been repeatedly stated, the prognosis in these cases is improved by the radical removal of the cause.

Facts Which Influence Prognosis.—The *neurasthenic and hysterical,* the *non-resistant, those who are burdened with an unfortunate heredity,* are likely to fall into a condition in which they are of no assistance to themselves in checking the advance of the disease. There are cases in which, in spite of energetic and radical treatment, the disease after an almost acute onset remains uninfluenced and progresses to the involvement and deep changes of many joints at once. With an acute onset as a rule the prognosis, however, is more favorable than in the chronic forms. In such cases, following the subsidence of the acute symptoms, the progression is likely to be slow. As a rule authorities have given an unfavorable forecast in cases which begin at the *menopause.* My experience has been that most of these cases advance to a condition in which the joint structure is moderately changed and then remain stationary.

It is exceedingly difficult to give a forecast though all data are at hand in the individual case, because of the vagaries of the disease and the variety of changes which may be included.

In all cases the *general condition* of the patient remains paramount. This is influenced by the *amount of pain suffered,* the *ability to use the extremities and jaw*—making proper *feeding* easy—and the *localization of the joint changes,* besides the *factors already mentioned.*

In the *atrophic type of the disease* the prognosis for restoration of function is bad. The joints are stiffened and malformed; hence their function is limited. Pain is a leading feature and makes the patient wretched and unable to enjoy life. He becomes depressed in consequence and presents a pitiful picture in contrast with the victim of the hypertrophic type of the disease.

The *hypertrophic arthritides* offer a relatively good prognosis: so far as life is concerned it is good; so far as restoration of function, it is bad. These patients are not bedridden; they are often able to help themselves and continue at their work, if it is not too strenuous. They often travel and are not discontented. The hypertrophy is likely to limit itself to one joint. There is no tendency to the disorganization and destruction of joint tissue which characterizes atrophic arthritis.

Herberden's nodes may be present for years unchanged, and with

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slight associated enlargement of a few smaller joints there seems to be no marked tendency to advance; neither do they cause noticeable inconvenience.

The *hypertrophic changes of the hip* (*morbus coxarius senilis*) in elderly patients already mentioned remain uninfluenced when once advanced.

Still's Disease.—Still's disease is in all probability a form of arthritis deformans occurring in children, the leading features of which are *chronic arthritis, enlarged lymphatic glands,* and *enlarged spleen. The disease is slow to progress and is periarticular—the glands and spleen are palpable.* The prognosis of Still's disease is not absolutely bad. I have seen marked retrogression of all the lymphatic glands and spleen and but slight final residual thickening.

The periarticular form of the disease is the most frequent and offers the best prognosis for ultimate usefulness and general health, though mixed types are not infrequent in the same subject.

Causes of Death.—In considering my material I have found intercurrent infection the most frequent cause of death, in those cases which have progressed and become practically helpless. *Pneumonia, tuberculosis, cystitis with bed-sores in neglected cases,* have been the leading causes of death. I do not in my series count a single death directly traceable to the disease. I have at present a patient in my wards who has been an inmate of the hospital and bedridden because of ankylosis over 25 years. His general condition continues good and he is the least troublesome patient in my service.

Blood and Urine.—Blood and urine analysis offer no data for prognosis in uncomplicated cases.

Climate.—Climatic conditions unquestionably influence the comfort of most arthritics. A dry warm climate seems most favorable; occasionally the disease has been stayed by a timely change.

Conclusion.—In offering a prognosis the attendant is never to be too sanguine of success in overcoming joint changes, in spite of the fact that he may have unearthed and removed the possible source of infection, for there may be multiple sources some of which remain undetected, or the destructive lesions in the joints are so far advanced as to offer no chance for improvement.

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C. Diseases of the Bones

1. *Osteitis deformans*

(*Paget's Disease*)

General Statements.—Our present knowledge of the pathology of excessive and purposeless deposits of bone is purely theoretical. We may finally find that these anomalies with family resemblances will be found with a single underlying cause, modified by varying conditions responsible for existing differences, including changes in bone of a rarefying nature and at the same time marked evidences of overgrowth—a combination which is now considered characteristic of osteitis deformans.

Virchow, in his "Krankhaften Geschwülste," gives a clear account of the many conditions in which there are bony changes now known as *hyperostosis, leontiasis, giantism, osteitis deformans,* and *Marie's hypertrophic pulmonary osteo-arthropathy.* Malpighi, as early as 1697, called attention to hyperostoses and overgrowths of the bones of the skull.

Sir James Paget, in 1876, first furnished a systematic rehearsal of the symptoms and pathology of osteitis deformans. The disease has since been known as "Paget's *disease.*"

Paget characterized the disease in his original paper as follows: "The disease affects most frequently the long bones of the lower extremities and the skull, and is usually symmetrical; the bones enlarge and soften; those bearing weight yield and become unnaturally curved and misshapen. The spine, whether by yielding to the weight of the overgrown skull or by change in its structure, may sink and seem to shorten, with gradual increased dorsal and lumbar curves; the pelvis may become wide; the necks of the femora may become nearly horizontal; but the limbs however misshapen, remain strong and fit to support the trunk."

The disease usually begins in middle life or later; its progress is exceedingly slow—requiring many years for its full development—and does not usually affect the general health. The inconveniences to which the disease gives rise are due to the changes of shape, weight, size, and direction of the diseased bone—as was shown in my cases (Elsner) in one of which the disease was not symmetrical but involved one-half the cranial vault (right side), including the right zygoma, the frontal, parietal, temporal, and occipital bones, directly to the median line. The left clavicle was three times its normal thickness; the right ilium was enormously

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enlarged while the right femur was curved like one-half of a yoke and thickened. The only history which bore on the etiology of this case was a fall on the head early in childhood. Not all cases progress to such full development, and as already suggested, symmetry characterizes the enlargement of the bones in most cases. I have reported two cases—my entire experience with the disease.

Paget gathered 23 cases before his death. Two cases were found at Johns Hopkins Hospital in 20,000 medical cases. X-ray pictures are characteristic. Packard and Steel have reported 99 cases of supposed osteitis deformans. They concluded that 66 of the 99 cases were authentic, and they added one of their own—41 were males, 24 females, and in two cases the sex was not stated. Both of my cases were females. My second case is the youngest reported, and was 12 when the enlargement of the rami of the jaws was first detected.

The frequency of involvement of the bones of the body are in the order following: the skull, tibia, femur, spine, pelvis, ribs, radius, and ulna.

In all cases when the skull is involved the spinal column yields and deformity results. The disease progresses gradually, but the deformity is so characteristic as to be striking. All of these patients with skull involvement look alike, just as myxedematous patients grow to resemble each other.

There is a striking *frequency of malignant growths* with hyperostoses. In Packard and Steel's cases (67) there were 5 with *sarcoma,* 3 *carcinomata* and 2 had *non-malignant growths complicating.* Therefore 4.5 per cent with cancer, and 7.5 per cent with sarcoma.

Mentally these patients with deformities of the head become depressed; they withdraw from society because they are hypersensitive. *Headaches* may become unbearable; ocular and aural disturbances are not uncommon. Four of Paget's 23 cases after many years became blind, one from *choroiditis* and three from *retinal hemorrhage.*

There are as a rule in most cases no evidences of cerebral compression. *I have found no history of a* case dependent upon syphilis—*none has been reported to yield to mercury or to the iodid.*

Diffuse hyperostoses which cause narrowing or closure of the foramina of the skull and associated pressure symptoms, such as blindness, exophthalmos or paralysis, are not to be diagnosticated as osteitis deformans. There will always be a certain number of "purposeless enlargements of bone" in which, because of close family resemblances, accurate differentiation cannot be made early; a limited number of these will progress. *Atrophy and absorption* is the ultimate fate of the bone in most cases of Paget's disease with consequent *weakening of the bony structure* involved, and compensatory *strengthening by the growth* of what may be looked upon as a variety of callus, the occasional formation of definite tumors

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and in some, fatal cachexia (Lunn). These views of Lunn are controverted by Sillock, Paget, and Butlin who lean to the theory that "the essential features of the osseous lesions of the disease are indistinguishable from, if not highly characteristic of, inflammation."

Duration.—Eltinge claims that "it requires from five to fifteen years to reach its maximum." My cases would extend that period. No treatment has the slightest influence in controlling the disease. If we adopt Adami's and Aschoff's views of the pathology that "there are two opposing pathologic processes at work, resorption and osseous hyperplasia," we must depend on nature's compensatory provision, by which the denser bone is finally deposited, not entirely decalcified, to stay the disease.

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2. *Leontiasis ossea*

(*Lion Face*)

Leontiasis ossea (Virchow) is a rare condition in which there is a diffuse hypertrophy of the bones of the skull, usually involving the bones of the face so as to give the appearance of the lion face. In the only case which I have seen in practice, the young man, age twenty, was otherwise perfectly well. Atrophic changes commenced in the teeth (upper jaw); gradually the alveolar processes receded and the maxillae thickened evenly. There were no further enlargements of the bones of the skull or body. In my case there was gradual progression until the recognition of the condition was easy even by laymen, and the young man become so embarrassed that he left his home town to escape his old comrades.

There is no way of influencing the gradual progress of the hyperostosis; it does not interfere with the general health of the patient. The process is held by some to be one of osteitis deformans. In reported cases it has continued from twenty to thirty years, and longer.

General hyperostosis of the skull (Prince) is also held to be a form of

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osteitis deformans from which it cannot be differentiated. Prince found in the cases which he collected from literature (21 in all) symptoms of *compression* as the skull increased in size—particularly of the foramina—leading to *neuralgia, blindness, deafness, bilateral facial paralysis* and more or less trouble in chewing and swallowing; in some cases there was paralysis which caused marked *respiratory embarrassment.* *Exophthalmos* has also developed in rare cases. These cases of enlargement of the skull are ultimately likely to develop *mental symptoms, marked depression, convulsions,* and *paralysis of the extremities.*

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3. Hypertrophic Pulmonary Arthropathy

(Hypertrophic Pulmonary Osteopathies, Clubbed Fingers, Hypertrophiante pneumique)

Hypertrophic osteopathies (arthropathies) are *always secondary* to other diseases, as was demonstrated by Marie in his study of his cases. The lesions within the lung were almost uniformly present; hence the condition is known as a "pulmonary osteoarthropathy." There is a symmetrical enlargement of the terminal phalanges of the fingers and toes with, in some cases, enlargement also of the distal ends of some of the long bones.

"Clubbed fingers" are recognized as frequent attendants of chronic pulmonary disease—tuberculosis particularly. Marie's description of 8 cases included thickening of the long bones near the joints with the characteristic deformity of the fingers and toes above mentioned. Four of his cases had pulmonary disease, in three the history was vague, and in one there was no evident relation to lung disease. Wynn found pulmonary disease in 68 per cent of his 100 cases, and Emerson quotes Alexander as having 77 of a total of 103 cases. Emerson reports 4 cases from the Johns Hopkins Hospital material in one of which there was empyema, one bronchiectasis, one chronic bronchitis and pleurisy, one with both bronchiectasis and pulmonary tuberculosis.

There are cases in which congenital heart lesions and acquired valvular defects are present without pulmonary lesions. Wynn reports 11 cases with hypertrophic cirrhosis of the liver. No tuberculous lesions need be expected in these cases in the changed bones. The real provoking cause remains problematic.

For a full clinical history of individual cases the reader is referred to Thayer's report of 4 cases from his clinic.

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As the enlargement of the bones progresses the surrounding tissues atrophy, and in some cases arthritis may be expected.

Hypertrophic arthropathy is not a disease per se; its prognosis must depend upon the nature and extent of the primary lesion. The "clubbing," which is the most constant clinical feature, does not interfere with the progress of the initial disease. In some cases there have been acute exacerbations with remissions and final long periods of chronicity, in accordance with the history of the benign pulmonary disease.

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4. *Fragilitas ossium*

Fragilitas ossium is also considered in connection with osteomalacia. With fragilitas ossium there is, because of a distinct nutritional fault, a tendency to fracture of one or more of the long bones. The bones are abnormally brittle. The change which leads to fracture may be due to secondary changes in the bone as the result of disease, local tumor, disuse, senility, locomotor ataxia, rachitis, chronic joint disease, the terminal stage of malignancy, phosphorus poisoning, scorbutus; or the condition may be *primary* without preceding disease or local lesion.

Deformities may result from the provisional callus following repeated fractures. In some cases of primary fragilitas ossium the bones, because of their chemically anomalous build, fracture on the slightest cause. Cases are reported in which as high as thirty fractures have followed each other in the same subject. There are no means of controlling the idiopathic cases. In cases of locomotor ataxia with fragilitas, I have imagined that the use of the lime salts (usually deficient) has been of some value.

Cases with hereditary tendencies may lead to fractures early in life; the prognosis so far as preventing recurrence of fractures in such cases, is not good.

Osteogenesis imperfecta.—In osteogenesis imperfecta, i. e., *fragilitas ossium of the fetus,* there are brittle bones which may *fracture in utero,* or there may be deformities due to the bending of bones. In such embryos the cranium is deformed. Death is the fate of most of these infants, though occasionally one escapes in whom with proper treatment, the nutritional fault is overcome and the bone growth becomes normal. The process of repair leads to good results in those who survive.

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Section IX

Metabolic Faults

1. Gout

(*Arthritis urica vel uratica, Goutte* (*French*), *Gicht* (*German*), *Podagra*)

Theories.—To consider the theories of gout, or the chemobiology of the disease in all of its protean manifestations fully, is not within the province of this work. I can only give an abstract of the leading theories which deal with uric acid formation, retention, and elimination, as related to the disease:

1. *Garrod* contends that an acute attack of gout is invariably produced by an excess of uric acid in the blood, due to increased formation and greatly decreased elimination; also that inflammation is caused by the deposition in the joints of sodium biurate.

2. *Haig* holds that there is a diminished alkalinity of the blood, and that the latter cannot therefore hold the uric acid in solution so that it is deposited in the form of urates.

3. *Ebstein* thinks it probable that there is primarily a cartilaginous necrosis, that the deposition of uric acid from the surcharged blood is secondary—with associated local inflammatory changes.

4. *Sir William Roberts* believed that acute attacks of gout are dependent upon the precipitation of the crystalline biurate of sodium; that the urate is transformed into the less soluble biurate in the blood; that normal blood or the blood of gout does not contain uric acid, as such, in solution.

5. *Von Noorden* concludes that the essential process is a tissue necrosis attributable to the presence of a hypothetic ferment, and that the uric acid, which is without etiologic effect, is deposited at the necrotic focus.

6. *Klemperer* has shown, as the result of observations made in cases of gout, that so long as the function of the kidneys is not materially interfered with, the presence of considerable amounts of uric acid in the blood must be attributed to increased formation. The presence of an equivalent of uric acid in the blood in other affections, however, than gout (e. g. leukemia) shows that this factor is not the sole cause of gout.

7. *Mordhorst,* in dealing with the pathogenesis of gout, states that in

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any alkaline liquid the basic substances combine with the uric acid, if this is present, to form a urate. These uratic precipitations are met in non-vascular tissues only, the alkalinity of which is less than that of the blood, and that they are the essential cause of the symptoms.

8. *Kolisch* maintains that the more serious features in gout, only exist in the presence of impairment of the renal function. When the kidneys are healthy, the alloxuric bodies are in great part increased at the expense of the uric acid. Chittenden and others hold, however, that the xanthin bases are practically free from toxic effects.

9. *Luff* thinks that uric acid is formed in the kidneys from a combination of urea and glycogen, an increased amount of the latter substance being formed in the liver.

10. *Brugsch and Schittenheim* contend that gout is due to metabolic faults which interfere with the conversion of the purin bases.

Conclusions.—The safest conclusion for the clinician to reach are that uric acid and the xanthin bases are derivatives from a parent substance, i. e., purin which possesses both basic and acid properties; further, that the purin bodies are characteristic products of decomposition of nucleoproteids and that within the body they arise from the nuclein taken with the food ("exogenous origin"), or they result from the katabolism of the body tissues containing nuclein (endogenous origin). Bains' conclusions are founded on these chemical facts, and for treatment and prognosis deserve to be kept before our mental vision. He regards the "uric acid phenomenon as an important incident" in gout though the "real or essential factor has so far eluded detection." The origin of the disease is probably in the alimentary tract.

Definition.—*I base my treatment of the prognosis of gout upon a broad definition which must include its acute and chronic anomalies which may be associated with both local and general symptoms at the same time.*

For all diagnostic and prognostic purposes *gout may be defined as a constitutional disease characterized by the deposit of the biurate of sodium in crystalline form in the cartilages and textures of the joints, including fibrous tissues associated with attacks of acute articular inflammation, systemic disturbances due in all probability to faulty conversion of foods and improper elimination, often associated with grave changes in the various organs of the body—preferably the heart, kidneys, and blood vessels.*

Gout is therefore a chronic constitutional disease in which uric acid formation and elimination are disturbed because of faulty metabolism. It is subject to acute exacerbations with intervals of apparent health, or its manifestations may be continually in evidence to make the victim a chronic invalid.

History.—The history of gout and its accumulated literature should prove of great interest to the student of medicine. Hippocrates described the disease 500 years B. C. Celsus during the first century of the Chris-

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tian era had a clinical knowledge of the disease, and Lucian in a satirical comedy proved the overpowering influence of the Goddess Podagra over mankind. The first accurate and systematic rehearsal of the clinical history of gout must be credited to Sydenham (1624-1689) which will always live as a classic in medical literature, than which there is no better guide to the differentiation of all forms of arthritis, nor is there a clearer presentation of the symptomatology of the disease (See Brugsch).

Causative Factors.—*Heredity.*—Heredity is the most important causative factor of gout. My cases show a positive hereditary tendency in 60 per cent. *Gout appearing before the age of 30 in subjects burdened with heredity is not thrown off.* Such subjects continue gouty throughout life. The disease is transmitted from generation to generation, though occasionally a generation may be skipped. There is a strong tendency toward transmission through the female line of the family to subsequent generations. Heredity will always prove an obstacle to a favorable prognosis though years may lapse without recurrence of symptoms after the initial attack.

Age.—In those who are strongly predisposed, gout may develop before puberty in rare instances. Sydenham and Heberden never saw true gout during childhood. Ebstein has reported *juvenile gout.* The larger number of cases are found during middle life (30 to 45 is the preferable period). It is not likely to develop after the fifty-fifth year. Of 180 men afflicted, Brugsch shows the percentage of first positive symptoms of gout as follows:

In	3	per	cent	the	patients	were	between	25	and	30	years
In	8	"	"	"	"	"	"	30	"	35	"
In	21	"	"	"	"	"	"	35	"	40	"
In	40	"	"	"	"	"	"	40	"	45	"
In	18	"	"	"	"	"	"	45	"	50	"
In	4	"	"	"	"	"	"	50	"	55	"
In	3	"	"	"	"	"	"	55	"	60	"
In	2	"	"	"	"	"	"	60	"	65	"
In	1	"	"	"	"	"	"	65	"	70	"

Sex.—Men are oftener afflicted than women; the latter when victims of the disease are likely to develop it after the menopause, when symptoms are often more or less continuous.

Habits.—Habits of life are important prognostic factors. Sedentary habits invite the disease, particularly in those with hereditary taint. When such individuals add to their inactivity errors of diet, live on rich foods and drink immoderately, all factors are combined to invite and continue the disease. *Alcohol,* particularly *sherry, port wine, champagne,* and the *heavy ales,* provoke the disease and acute exacerbations, particularly in the predisposed. The *distilled spirits* are better borne than are the heavy wines.

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Idiosyncrasies to certain foods are frequent in the gouty. *The study and rational treatment of such cases will often prevent the persistence of atypical symptoms and the recurrence of regular attacks of acute gout.* A diet composed largely of *carbohydrates and proteids* (including purin bases) with *improper exercise and faulty ventilation* may include the underlying exciting cause of symptoms. *Overeating* will certainly prove an important factor which, when discontinued, often changes the picture satisfactorily. The English, probably because of their excessive beef eating and ale drinking, are more subject to gout than are the Americans. It is less prevalent in Germany than in England.

Lead Poisoning.—Garrod reports that 33 per cent of his cases had *lead poisoning.* Oliver noted that "lead workers in the southern part of England developed gout in the northern part of England, whereas the natives under the same conditions seldom became gouty even though the kidneys were affected." Bain noted: "In districts where gout is unknown, the disease does not appear to be provoked by lead poisoning, but gouty persons are particularly susceptible to the influence of lead even in medicinal doses."

Lowered Standard of Health.—Gout is, in the gouty, hastened by the *lowering of the standard of health,* by *depression, grief, sorrow, continued worry; fatigue* has been a frequent cause of recurring symptoms. *Faulty homes,* continued living in *damp houses* and *exposure to wet and cold,* and *in some, minor factors without effect on those with normal resistance,* prove sufficient to aggravate existing latent gout to activity or to cause acute attacks.

Gout may be:

(a) Acute gout
(b) Chronic gout
(c) Irregular (abarticular gout—metastatic gout).

(a) Acute Gout

Initial Symptoms.—The initial symptoms of acute gout are fiery and painful; there is usually considerable febrile disturbance; the "sthenic condition" is predominant, while the local manifestations are characteristic. These symptoms, while associated with some acceleration of the pulse and often increased tension, with temperatures between 101° to 103° F. or higher, are without serious import and yield in the course of a few days. The *urine* is concentrated and reduced in quantity, may even contain albumin with an occasional cast (hyaline or epithelial), in a subject who before had no urinary anomaly. The prognosis under these conditions without added complication is good.

In my experience *added infection* or *serious complication* during the persistence of acute exacerbations of gout has been exceedingly rare.

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Evidences of Approaching Remission.—The evidences of approaching remission include free perspiration, increased urinary secretion, fall of temperature, relief from the severe pain and local joint swelling.

Course of the Disease.—The prognosis is best for prompt subsidence of symptoms in *monarthritic cases* (big toe usually) which commenced with free outspoken symptoms, usually high temperature. When, as occasionally happens, one large and several smaller joints are acutely attacked, the symptoms yield slowly. The limitation of acute gouty inflammation to the smaller joints of the hands and feet is not frequent; when it appears, convalescence is slow. In over 70 per cent of my cases the joint changes during the initial acute attack were limited to the first *metatarsophalangeal articulation of the big toe.* Following the acute attack, the patient may appear to be in perfect health; will be able to return to his work somewhat reduced in flesh but without permanent damage to the joint, though it may continue tender during several days or weeks.

Duration.—The average duration of the acute attack is between three and six days. *Acute exacerbations in chronic cases are likely to recur;* it is impossible to foretell when these acute exacerbations will recur. There are patients who always have "twinges," who have insignificant or persistently annoying evidences of chronic and irregular gout, who may live during many years without acute joint symptoms. On the other hand, patients with evidences of persisting atypical gout may at short intervals develop acute gouty arthritis—limited to one or more joints. In some, there are no "interval symptoms" of gout, but recurrence after short respite cannot be prevented.

In cases of recurring arthritis the joint structure shows organic change and chronic gouty arthritis develops to continue during life. When such changes have followed, *tophi,* the characteristic sodium urate deposit of gout, will be found studding the ear (helix) and other parts of the body.

The shorter the interval between the attacks, the longer the acute exacerbations, the more likely are organic changes in the joints to follow. With associated irregular gout in the intervals, with cardiovascular and renal complications, the worse is the prognosis for full restoration to health.

Determining Symptoms.—*Persistent albuminuria with high blood pressure,* or the latter alone with *slight hypertrophy of the left ventricle,* must lead to the suspicion of associated *nephritis*—probably interstitial—and the prognosis given accordingly. The *urine analysis* is of great value in the prognosis of the acute attack. With diminution of uric acid and the alloxuric bodies in the urine of the gouty individual which has been cautiously watched, an acute attack may be anticipated; with the reappearance of the normal balance or the increase of uric acid output the attack may be expected to yield. Naturally during the attack the uric acid of the blood shows increase (Garrod thread test) (Maase-Zondek Test).

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The acute attack may occasionally lead to recognizable *anemia,* which is not likely to continue long. This is more likely to follow after repeated attacks at short intervals and should always arouse a suspicion of possible nephritis.

During the acute exacerbation there is usually some *leukocytosis* with moderate *eosinophilia. Polycythemia* in obese and plethoric subjects has been noted; these are often without satisfactory resistance. DaCosta reports one case in which the red blood corpuscles numbered 7,125,000 in the c.mm., the whites 14,000, hemoglobin 100 per cent, and myelocytes 4 per cent.

(b) Chronic Gout

As already suggested, acute gout may lead to a chronic gouty state in which repeated acute exacerbations are to be expected. *Chronic articular gout is a persistent arthritis* in which the joint structure is changed, and never returns to a normal condition. In most cases of chronic gout there are *extra-articular lesions* which are included in the complex of irregular gout, and the *length of life in such cases depends more upon the associated lesions than upon arthritic changes.*

With limitation of gout to the joints and but slight cardiovascular or renal disturbances, these patients may live for years in comparative comfort. Indeed, *Heberden's nodes* with limited change in joints may argue in favor of the long life of such gouty subjects.

Ulcerative articular processes in chronic cases, unless leading to sepsis, may heal or remain without bad results. Such processes are usually limited.

The disorganizing and destructive changes within the joint are permanent. The *extent of the joint changes* naturally influences the life of these subjects and with marked pain, tenderness, swelling, distortion, destruction, and added irregular gouty symptoms, they may become bedridden or so handicapped as to make locomotion impossible.

The assistance which x-ray examination gives for prognosis may be valuable in such cases as are associated with cardiovascular changes and other symptoms suggesting renal calculus, in which positive diagnosis for relief of the accompanying and threatening complications becomes necessary.

Anchylosis and muscular atrophy remain practically uninfluenced by treatment.

(c) Irregular Gout

(Abarticular Gout)

Gout may affect almost any organ of the body without showing change in a single joint. This is not the rule but it is oftener true than is generally believed by the average clinician.

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Complications.—*Gouty disturbances of the nervous system* (*neurasthenia, neuritis*) recognized early and radically treated offer an excellent prognosis (See Neurasthenia). *Migraine* of gouty origin is controlled with great difficulty—often entirely uninfluenced. *Arterial degeneration* resting upon a long-continued gouty fundament is a frequent complication and in uncontrolled cases is associated finally with *ventricular hypertrophy* and *kidney involvement* (*chronic gouty kidney—chronic interstitial nephritis*). The prognosis of these conditions is separately considered. When lesions are advanced it is unfavorable. Patients with "gouty hearts and kidneys" may live many years in comfort, even to old age, with proper care. They demand watching and always stand on the edge of a precipice.

The small trace of albumin with an occasional hyaline cast in the patient after fifty, who may or may not be of gouty habit (*usually he is*) *may prove beneficial, for it often leads to right living with consecutive prolongation of life.*

Irregular gout including any of the preceding complications, with myocardial degeneration, with coronary or mesenteric sclerosis, with diabetes mellitus (a frequent complication of gout in such subjects) offers an unfavorable forecast. *Diabetes mellitus* in obese, gouty subjects without other serious complications does not lead to early death when recognized and rationally treated. Some of these subjects reach old age. That the presence of the diabetic condition is a handicap, cannot be denied. I *have seen patients with gouty kidneys, low specific gravity urine, live to old age.* Complications (uremia, pneumonia, and other infections) are to be feared. *Amyloid disease* develops in some—it is always fatal and general.

Gout, as it influences digestion—*gouty dyspepsia—is usually secondary to some other condition—hyperacidity* or *faulty renal elimination.* It may be functional and associated with marked neurasthenia. The prognosis depends upon the ability to regulate the patient's life and mental processes.

Pyrosis, flatulence, constipation and other *gastrointestinal symptoms* are in most cases easily and favorably influenced. It is surprising to note how the relief of constipation or an occasional free catharsis improves the gouty subject during a considerable period. The *functional symptoms referable to the heart in irregular gout are usually relieved by the treatment of the gastro-intestinal tract and attention to the urinary secretion.*

The *skin lesions* of gout are often rebellious, but in the end are likely to yield to rational living and proper diet. Recurrences are frequent, often during long periods. They include *eczema, erythema, urticaria, pruritus universalis et genitalia.*

Stone in the bladder and kidney of gouty origin offers a favorable fore-

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cast when recognized early, in the presence of a good resistance and the absence of cardiovascular and renal changes.

Gouty subjects with *enlarged prostates and cardiovascular changes, also nephritis* (interstitial), do not bear prostatectomy well and often die within the first twenty-four or forty-eight hours following operation, with evidences of deep uremia.

Gouty bronchitis, asthma, and *emphysema* are best influenced by climatic change. Often they continue rebellious to any other treatment. *Pericarditis* may prove an occasional serious complication. The *changes in the endocardium are less likely to be of inflammatory than degenerative origin and are a part of the arteriosclerotic process.*

Tuberculosis may be invited in the gouty subject, particularly the younger with bad heredity, who early develop deep joint changes and who live under unfavorable conditions. Tuberculosis in gouty subjects is likely to have *early hemoptysis* which may not recur; in gouty subjects it is, as a rule, exceedingly chronic (See Stockvis, Pollock, Pye-Smith and Moore).

Moore reports, in 80 gouty patients, 3 gall-stones and 6 with pulmonary tuberculosis.

Gall-stones and *cirrhosis of the liver* have been noted in a comparatively large proportion of cases (Murchison).

Gouty invasion of the eye is often slow to yield; is subject to recurrence; may lead to adhesions (iritis), and with arterial involvement, to retinal hemorrhage. The inflammatory conditions as a rule are fully healed.

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2. *Diabetes mellitus*

General Considerations.—Whenever there is faulty metabolism dependent upon organic changes in one or more organs, discoverable or not, with more than 0.2 per cent of glucose in the blood and more than 0.1 per cent—0.2 per cent in the urine, both persistently present, it may be safely concluded that the patient is suffering from *diabetes mellitus.*

In considering the prognosis of diabetes mellitus there are a number of underlying facts which deserve accentuation:

Our exact knowledge of the most important facts bearing upon the chemo-biologic processes and pathologic anomalies which perpetuate glucosuria and which finally lead in most cases, to innumerable symptoms, is limited.

We do know that the liver stores carbohydrates to convert them into glycogen to be ultimately delivered to the blood as glucose (grape sugar), thence to the tissues for final oxidation (Claud Bernard). This theory has never been successfully controverted.

An *excess of intake of sugar* may produce glucosuria (See Alimentary Glucosuria). Claud Bernard established the fact that *lesions of the floor of the fourth ventricle* in the medulla produced hyperglycemia and glucosuria. We know that nervous influences increase symptoms in diabetics; we do not know whether without added alimentary conditions a true chronic neurogenous diabetes can persist.

Factors in Producing Glucosuric Condition

Pancreatic Disease.—*Pancreatic disease or injury is the most constant pathologic attendant of diabetes mellitus;* the usual change is a far-

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reaching *fibrosis,* though other pathologic processes both acute and chronic may lead to the symptom complex.

Opie, von Mehring, and Minkowski have established the fact that glucosuria may be produced experimentally by the removal of the pancreas; particularly the "islands of Langerhans" which furnish an internal secretion needed for the normal conversion of carbohydrates. *There are but few, probably no cases of diabetes mellitus without pancreatic insufficiency.* For prognosis it is important to recognize the fact that *in children there is* (as von Noorden holds) *progressive atrophy of the islands of Langerhans.* Hence the prognosis is bad during early life. *In adults,* pancreatic function may during limited periods be restored, the process of fibrosis or degeneration may remain stationary, or there may be compensatory changes which lead to material improvement; under stress or injudicious diet glucosuria may return, but it may be absent during encouragingly long periods.

Adrenalin.—Herter established the *relations of the suprarenal substance* (adrenalin) *to glucosuria.* He found that if the pancreas is painted with a solution of adrenalin chlorid a transient glucosuria results with corresponding glycemia, while no glycemia or glucosuria follows a similar application to the spleen or liver. Once the chlorid undergoes oxidation the power to produce glucosuria or to raise blood pressure is lost. *Adrenalin poisoning causes granular degeneration of the islands of Langerhans. Glucosuria is not uncommon with suprarenal disease.*

Diabetes Bronzé.—*Diabetes bronzé,* a condition which is fatal, in which glucosuria is present with *pigmentation of the skin* and *cirrhosis of the liver or other productive changes, is uniformly associated with pancreatic anomalies* (See Aschoff) *and hemochromatosis. Suprarenal secretion* is intimately concerned in the control of liver function. "It is the second of the guards placed over the liver which regulate the excitability of the sugar factory" (von Noorden).

Disease of the Hypophysis.—*Disease of the hypophysis* (Cushing) particularly *tumors, acromegaly* and *trauma* may cause glucosuria. Cushing has demonstrated experimentally the influence of the posterior lobe of the pituitary in carbohydrate metabolism. 35 to 40 per cent of acromegalics show sugar (Borchardt).

Administration of Thyroid Extract.—The association of *glucosuria* or *true diabetes mellitus* with *exophthalmic goiter* and the production of glucosuria following the administration of *thyroid extract* are frequent occurrences. von Noorden says "probably the parathyroids also stand in metabolic relationship to the pancreas."

Diseases of the Liver.—Most *diseases of the liver* in which glucosuria persists are associated with pancreatic disease (organic usually). Naunyn has observed cases without pancreatic lesions. I have seen cases in which recurring glucosuria was present with *gall-stones* which disappeared after

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operation or passage. *Acidosis is not a frequent accompaniment of diabetes, which seems to depend upon liver degeneration.*

Traumatism.—When traumatism has seemed to be a factor in the production of glucosuric conditions *brain injury* has, in my experience, been the cause. Grave symptoms of fracture or concussion have been prompt, sugar was demonstrable early, and the course of the disease rapid. *Without evidences of grave injury the presence of sugar may be attributed to preceding disease.*

Skeletal Muscles—Proteid and Fat.—*Sugar does not provide the only source of glucose in the blood for it may be formed from the proteid and fat elements* ingested; in diabetes, particularly in the malignant types, also during *starvation,* the *skeletal muscles* and the remnant of fat furnish it under the "changed metabolic relations." "The liver uses fats for the purpose of forming sugar only when the poverty of other materials makes it necessary" (von Noorden). These facts have an important bearing on prognosis, particularly as it is related to the rational dietetic treatment of the individual case.

Negative Factors

Kidney.—Probably the kidney itself is not an important factor in the production of glucosuria. With *phloridzin poisoning* or its injection into animals (*phloridzin glucosuria*), when renal lesions are present as the only accompaniment of organic change, there is never hyperglycemia as in ordinary diabetes mellitus. The kidney has simply lost its ability to prevent glucose elimination. The presence of *nephritis* in *gouty subjects* with diabetes mellitus does not argue in favor of the former (nephritis) as the provocative factor in causing the latter; both are dependent and secondary to the same constitutional fault, though one may aggravate the other and influence the prognosis.

Contagion.—In spite of Senator's suspicions, diabetes mellitus can never be considered to be contagious. The reports showing the relative frequency of the disease in husband and wife may for our purpose be considered coincidence only—possibly dependent at times, upon the same improper diet or other unknown factors.

Alimentary Glucosuria

There are transitory forms in which the urine, during limited periods, and the blood as well, contain more than the normal sugar content known as *glucosuria*—of which *alimentary glucosuria* is the most prominent example.

Tolerance.—The tolerance to assimilate sugar is not the same in all subjects. *Persistently low tolerance* is abnormal—occasional intolerance may not be. When there are *repeated evidences of intolerance* (re-

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peated alimentary glucosuria), *particularly in those predisposed* (heredity, etc.) *cautious watch should be instituted, for finally in the majority of these cases diabetes mellitus develops.* Prognosis of repeated alimentary glucosuria must be guardedly given and only after a sufficient period of observation which leads to the determination of the tolerance of the subject, which is not always the same even under normal, and unchanging conditions. Hofmeister, however, holds that for the same individual and the same carbohydrate, the tolerance varies so little as for practical purposes to be considered unchanging.

Large quantities of sugar given on an empty stomach to normal individuals will produce glucosuria promptly, and this is of no prognostic significance *per se.* Naunyn has established the fact that the normal tolerance of man makes it possible to take larger quantities of sugar into the full than into the empty stomach without causing glucosuria, due to the more gradual absorption of sugar under such circumstances and the consequent slower flooding of the blood.

The tolerance varies between 50 and 200 grams under different conditions. The normal subject can tolerate 100 grams of sugar without recognizable glucosuria two hours after a breakfast of coffee with milk and 100 grams of bread (Naunyn).

Origin.—*True alimentary glucosuria* is often of *functional origin* when, as not infrequently happens, in the predisposed and neurasthenic with traumatic neurosis, at times glucosuria develops, also with brain anomalies (meningitis, debility, mania and paralysis) (von Noorden); or there are *pancreatic disturbances of a transitory nature* in which, for some unexplainable reason, function is disturbed in which there is because of *faulty stimulation,* marked inability of the liver to store glycogen. In all of these conditions we may assume theoretically that the liver proves itself inadequate when excess of sugar is suddenly brought to it from the portal vein. It is by no means easy to cause alimentary glucosuria in the presence of organic disease of the liver through levulose, as Strauss has demonstrated, easily passes into the urine in all diseases of the liver, and *alimentary levulosuria* is conceded to be evidence of liver insufficiency—*"insufficience hepatique."*

Relation to Diabetes.—*The development of glucosuria from the ingestion of starch should be interpreted as being pathologic.*

When glucosuria recurs persistently, in spite of intervals of freedom, suspicion of the presence of diabetes mellitus in its incipiency is justified and prognosis should be given accordingly. With a bad family history this forecast is strengthened. *It often happens that with hereditary predisposition* there are repeated periods during which there is supposed alimentary glucosuria.

Relation of Lactosuria to Diabetes.—Lactosuria found during pregnancy, after childbirth, during a limited period following weaning from

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the breast, is not of serious import; it continues but a short time, and bears no relation to true diabetes.

Glucosuria Following Drinking of Beer, Etc.—*For insurance examiners it is important to emphasize the insignificance of transitory alimentary glucosuria after the drinking of beer, champagne, and other sweet drinks excessively, in some even in limited quantities. In all such cases a period of observation is needed to clear the diagnostic horizon.*

Glucosuria Following Anesthesia.—The appearance of glucose in the urine, after anesthesia (chloroform, ether, etc.) or *coal gas poisoning,* is not *per se* of serious significance. *Deep narcosis in the presence of fully developed diabetes* often exerts an unfavorable influence on sugar elimination.

Factors Which Influence Prognosis of Diabetes

Heredity.—*Heredity is one of the most prominent features of diabetes and when present influences the case unfavorably as a rule,* though many exceptions to this conclusion have been filed by competent observers. The history of diabetes in the family was found in 20 per cent of my cases. I have the records of as many as five diabetics among the children of a diabetic parent. The disease in several brothers and sisters is strikingly frequent. *Most inherited diabetes is associated with the neuropathic disposition. Long continued worry, sudden shock, emotion,* and *acute infection* are factors which hasten the disease in those burdened by an unfortunate heredity. Among young children heredity is particularly striking; I have seen three brothers—all less than five years of age—die of the disease.

Sex.—The majority of diabetics are men—possibly the average proportion from all collected statistics is three to two. My material shows 118 diabetics among 6,300 internal disease—about .2 per cent—of which there were 80 males and 38 females. The prognosis under like conditions is not affected by sex; men are more exposed to the infections, are less able as a rule to care for themselves than women, and are also less amenable to treatment (diet, etc.).

Age.—The influence of age on the prognosis of diabetes mellitus is powerful. The general rule may be accepted which holds that before the tenth year the disease is uniformly fatal, and death follows within a limited period; that from ten to twenty-five the disease is almost always fatal, though its duration is longer and it is more amenable to diet than during the first decade of life; that from twenty-five to forty the prognosis is less favorable for control of both glucosuria and glycemia than later in life; that the complications due to infection and hyperglycemia are, with acidosis, the most frequent causes of death; that the prognosis for the prolongation of life after the forty-fifth year is far better than before, provided the disease is recognized early, is rationally treated and the neu-

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ropathic habit is not in the ascendency, the dangers of infection are escaped and there are no complications which undermine the resistance of the patient. In other words, it is plain that *in young subjects tolerance for carbohydrates once reduced to cause diabetes cannot be re-established unless due to a removable cause.*

Riesman, speaking of the mild diabetes in children, says that *mild diabetes in children* may be successfully treated. He reports four cases in detail which responded to diabetic treatment; all recovered. He believes that there may be several cases in the same family without the usual collateral symptoms of diabetes; they are mild cases and get well. I have had no such favorable cases to treat in my practice.

Control of Hyperglycemia.—True diabetes and its complications depend very largely upon the control of hyperglycemia (sugar in the blood) because it is the leading factor in causing the disorganizing and degenerative changes in vital organs. *Young subjects, because of failure to control metabolism, are prone to the early development of acidosis.*

Race and Geographic Location.—Jewish patients outnumber all others in their tendency to develop diabetes. They were found by Frerichs to include over 25 per cent of all cases. Naunyn, Osler, Tyson, and most authorities offer the same conclusion. Negroes develop diabetes but not with the same frequency as do whites. The prognosis of the disease *per se* is not influenced by racial factors, though among Jewish patients with overpowering neuropathic habit, emaciation is often rapid and polyuria prominent—conditions which unfavorably influence the outcome, for they shorten life. The mortality statistics of Prussia during 1897 showed 6-7 times as many deaths among Jews as Gentiles, and 1.1 per cent of all deaths among Jews were due to diabetes.

Dickinson in his monograph holds that the disease is more prevalent in the country districts of England than in the cities. In central New York the relative frequency of diabetes among farmers has unquestionably increased, and this increase holds for the diabetes of early life as well. Light complexioned races, Scandinavians, are prone to the disease, though the disease is more frequent in Southern Europe, Italy, also in India, than in Russia, Holland or in South America—Brazil particularly. Diabetes is increasing in frequency in all civilized countries; this fact is demonstrated by life insurance statistics and the material which is admitted into the general hospitals of our own country and Germany. During two three year periods the Germans report:

During 1877-1879:
Total number patients admitted 1,330,000—Diabetics 575.

During 1905-1907:
Total number patients admitted 4,560,000—Diabetics 10,725.

The increase in admissions was 3.3 times greater; the number of diabetics 19 times greater.

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Diabetes in Infancy and Childhood

von Noorden says: "With few exceptions diabetes in childhood knows no cure, no matter how mild it may appear in the beginning nor how gradual its development in the first months or even years." Cases reported as cured among children are not true diabetes mellitus. *There have been cases reported as cured in which there was unquestionably transitory glucosuria, others in which long periods of latency proved misleading.*

Transitory and alimentary glucosuria in children may disappear permanently but cases of "so-called alimentary glucosuria" in children are exceedingly rare and should be cautiously watched. In the end, it will be found that most are true diabetics. *Intolerance for carbohydrates may show itself early in life, may persist, but in some cases may never lead to true pancreatic diabetes.* In children the cardinal symptoms—thirst, polyuria, emaciation, hunger, with sugar in the urine are prominent early, and in most cases make diagnosis positive. My experience with the diabetes of early life has been comparatively large and as stated above, not a single case has lived; *most have died of acidosis within the first six months* following the detection of the disease, but few have lived an entire year; none were alive who were less than six years old at the end of 18 months. In cases between 15 and 25 I have occasionally met long periods of latency. In one such case I was tempted to change my diagnosis. A young man aged 17 was losing between 3 and 5 per cent of sugar. Under hospital treatment he was taught to diet; he became "sugar-free' during five years, so far as could be determined. At the end of the fifth year he presented with all of his original symptoms, marked acidosis, and died in coma enormously emaciated in a few months. Such experiences are occasionally repeated and need correct interpretation.

Diabetes in the Obese

(See also Obesity)

When obesity has been extreme and diabetes persistent with albuminuria, the feature which is finally added and most serious has been *myocardial insufficiency.* These patients often live many years uninfluenced by the glucosuria but they are bad risks, and with increasing dyspnea are ready for one of many further complications which may end life. My cases have usually died of degenerative rather than direct toxic processes.

Obesity with gout and diabetes offers an unfavorable prognosis so far as life is concerned, with associated degenerative changes, but moderately fat people with limited gouty disease may live many years.

Obesity with mild diabetes without associated disease or other complications may persist many years, and these patients may die of intercurrent disease.

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Obesity, arteriosclerosis with or without heart lesions and diabetes, may remain stationary during long periods or may progress with surprising rapidity. Such patients are always uncertain of their future.

Acute Diabetes mellitus

Acute diabetes is more frequent than has been supposed in the past, though it is comparatively a rare disease. I have examined the first thirty volumes of the Transactions of the London Clinical Society and find but one case (Hale White) of acute diabetes reported. The disease may present so suddenly without prodromata as to prove puzzling to the diagnostician.

My experience includes 8 cases during 30 years. All of these died within ten days, most before the end of seven days. Two were in adults, both males, 30 and 45 years of age respectively; five were in children less than ten years of age, and one was in a girl aet. 15, in whom there was sudden acidosis with rigid abdomen over the pancreas and enormous sugar loss. In all the polyuria and "melting away" was striking. The oldest patient—aet. 45—was perfectly well prior to exposure to cold and wet, and died in coma before the end of the seventh day. Besides the glucosuria and the fulminating course (there was no doubt of his previous good health) the enormous polyuria, specific gravity between 1,015 and 1,025 (1,000 c.c. every two hours during the last days of his life), and complete paralysis of the bladder were the leading features. *In the cases of acute diabetes in the younger children, exposure to extreme cold was unquestionably responsible for two deaths.* One case seemed to follow worry over approaching school examinations; in the other case the cause was not suspected. The urinary evidences in all acute cases are positive; all have polyuria and acidosis; all die.

Chronic Diabetes mellitus

The Relative Value for Prognosis of Individual Symptoms

Duration.—There is no time limit to mark the duration of chronic diabetes. Deaths during the first or second year are uncommon—thirty years and longer are not unusual periods for the continuance of symptoms.

Hunger.—*Persistent hunger,* which remains unrelieved by rational diet, which is associated with progressive emaciation, offers an unfavorable forecast for control of the disease.

Normal appetite, with *gain in weight* after the detection of the disease and favorable influence on the sugar loss, offers an encouraging outlook.

Abnormal appetite with great *thirst* and *polyuria,* usually with *persistent diacetic acid* in the urine with or without albumin, is unfavorable

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and death is not long postponed in such cases. This is particularly true when with the above complex there is also *hurried respiration*—a symptom of *acetone poisoning* always threatening when present.

The safest diabetic is the one whose appetite remains normal, whose sugar loss is not markedly increased, easily controlled, and *who "holds his weight" without the development of cardiovascular or renal complications.*

Thirst.—*Persistent thirst after a reasonable period of rational diet,* with or without marked change in the sugar loss, should always call for a guarded prognosis.

Relief of thirst by diet and the return of the urine to approximately normal conditions, the relief of polyuria, if present, are favorable. Persistent thirst with progressive loss of weight—no matter what the sugar loss, is never favorable and these cases, though sugar may for a time disappear entirely from the urine, are likely to develop acetone poisoning, and die.

Emaciation.—The initial loss of weight *per se* in an undetected and untreated case should not materially influence prognosis. If the case is not acute, the prognosis should be held *sub-judice* until the patient has received dietetic treatment. *Progressive loss of weight with persistence of hyperglycemia and other cardinal symptoms is unfavorable.*

Increase of weight or *stationary weight* which approaches the normal of the individual argues in favor of control. With *added chronic infection, particularly tuberculosis, loss of weight* is likely to be rapid and the process promptly destructive of lung tissue with high temperature, rapid and increasing heart weakness, and early death.

Polyuria.—In the average case of true diabetes there will always be a tendency to increased urine secretion so long as the glucosuria remains uncontrolled. *Slight increase of urinary secretion with small sugar loss in chronic diabetics without complications may continue during many years without materially influencing the comfort of the patient or his general condition. Polyuria which continues uninfluenced by diet,* no matter what the specific gravity of the urine or the amount of sugar loss, should always lead to the suspicion of serious complication, *uninfluenced hyperglycemia, chronic interstitial nephritis,* or *grave central nervous disease.* It always demands a cautious prognosis.

Control of polyuria with improvement of other cardinal symptoms is among the favorable features of the disease.

Pulse and Blood Pressure.—*Persistently rapid pulse, arhythmia, erratic or delirious hearts,* are unfavorable. *The tendency of chronic, particularly uncontrolled diabetes, is to cause or to be finally associated with heart and arterial change.* The longer these are postponed, the more favorable is the prognosis for life. After middle life *arteriosclerosis* and *diabetes mellitus* are often associated and may persist unchanged during long periods under favorable conditions (proper living and diet). The prognostic data associated with the pulse must be considered in connec-

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tion with the vital organs likely to be changed because of long continued irritation (hyperglycemia). My clinical material demonstrates that *diabetes mellitus is not a hypotensive disease*—the cases have, as a rule, when beyond the early stage, shown normal or approximately normal systolic pressure. As the disease has advanced in those beyond middle life with the associated *arteriosclerosis* and *cardiac hypertrophy,* there has been higher systolic pressure—usually between 160 and 180 mm. Hg. In these cases the diastolic reading has been relatively low—pulse amplitude has consequently averaged between 60 and 80 mm. Hg. This is probably due to the associated cardiovascular and renal complications of the disease when it has existed long in those beyond the meridian of life.

Persistent *gastro-intestinal disturbances* with *dry tongue, decaying teeth,* and *gingivitis* is an unfavorable combination.

The Mental State.—The fact that diabetes mellitus has persisted during many years, at times with appreciable sugar loss uncontrolled and often in the presence of arteriosclerotic changes, should not lead to the conclusion that these subjects are mentally incompetent or that they lack testamentary capacity. The majority of diabetics until they develop the final, fully developed diabetic coma, are alert, mentally active and normal, unless they suffer from chronic toxemia. *Pronounced mental hebetude* due to acetonemia is likely to remain uninfluenced during long periods; if relieved it is likely to return. Those who begin with mental symptoms usually run a rapid course for they are poisoned early (See Diabetic Coma, Acetonemia).

Acidosis.—*Acidosis* (Kussmaul) *has ended the lives of over 60 per cent of my cases; all acute diabetics have died of it.* Acidosis results from the faulty consumption of the fats. *B-oxybutyric acid* is the important factor in the production of diabetic coma and the alarming symptoms of poisoning—acute and chronic—which terminate the lives of many diabetics.

When acetone is present, diacetic acid is reasonably certain to show in the urine. The latter is easily detected by the ferric chlorid test. The most convenient test for the busy physician for acetone is known as *Garrod's modification of the Rothera test.* (To 5 c.c. saturated solution of ammonium sulphate add 5 c.c. of the suspected urine, then 3 drops of *freshly* prepared saturated solution of sodium nitro-prussid, and finally 2 c.c. of ammonia. Acetone will, if present, gradually develop the permanganate color which is positive and not shown by anything else.)

In all cases of acidosis the prognosis will depend upon the severity of the toxemia, the resistance of the patient, the associated complications, the recognition of the condition early and its prompt and thorough treatment (Gordon).

In young subjects acidosis once developed is not likely to yield, if it is associated with symptoms of deep involvement of the sensorium.

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There are cases of *chronic acidosis* in which the urine always gives characteristic reaction—at times in the absence of glucose—which live during long periods but they are always in danger.

Acetone poisoning may develop and prove serious in the chronic severe cases when a too rigorous diet has been insisted upon. Such cases may fall into deep coma without prodromata, and promptly die.

Profound acidosis in chronic cases may yield to alkaline flushing. I have seen several such cases in which life was prolonged during several years. In the end these patients are likely to die in coma. *Hurried respiration in the diabetic should always arouse the strong suspicion of acidosis. In children this is one of the positive and most frequent symptoms of acidosis and persists until death,* which usually follows promptly. In these cases the sweetish breath, as in all acidosis, and the sunken eye with pinched facies and emaciation are characteristic. *Insomnia* and *other mental symptoms,* some transitory, may be traced to chronic acetonemia.

Muscular Weakness.—*The marked and suddenly arising weakness of the chronic diabetic is often due to acetone poisoning, large sugar loss, or some complication.* The weakness may prove persistent during considerable periods. The extreme *muscular weakness* in mild or medium cases is usually not persistent. *Extreme muscular weakness with persistent acidosis* is always unfavorable.

The Urine.—I have in the preceding paragraphs referred to polyuria and its prognostic significance.

The *quantity of urine* voided, the tissue destruction and faulty oxidation, of which it proves a reliable index if cautiously studied, are important prognostic factors. Urine which is persistently of high specific gravity, particularly when the sugar loss is high, with or without evidences of acidosis, in the presence of other cardinal and uncontrolled symptoms, indicates severe diabetes. *The urine is the most reliable index of the influence of diet on sugar loss; at the same time its cautious examination makes possible the early recognition of associated toxicity*—an elementary statement—but one which requires repetition because of the repeated failure of the clinician to take advantage of the laboratory to assist him throughout the treatment of these cases. *It is not always possible to prognosticate from the amount of sugar present, for there are innumerable cases which during long periods lose relatively large quantities of sugar and live without complications.* In some, the sugar is finally reduced and may persist at an unchanging level during years. *The sudden disappearance of sugar in the severer forms is ominous and may precede acidosis.*

The *presence of small quantities of sugar* as shown by frequent *polariscopic examination* in the majority of cases without complications, which are cautiously treated, may not in any way interfere with the general health. The ridding of the urine of sugar when associated with

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general improvement and the control of leading symptoms is always favorable.

The presence of an *occasional trace of albumin* without more than a hyaline cast after the age of fifty in a diabetic urine requires watching but is not to be interpreted as of serious import. Urine which is characteristic of *advanced nephritis* (chronic interstitial) with sugar, is usually evidence of arteriosclerosis and myocardial change (hypertrophy)—all likely to develop in many of these cases.

The Blood:—The method of Bang for the *estimation of sugar in the blood* is probably the best we have, but it is too complicated for the busy clinician. The mischief which hyperglycemia is doing in the individual case is best interpreted by its clinical features (thorough physical examination) and repeated urine analysis. The blood itself deserves cellular examination in all cases. In the severe cases there is marked polycythemia (as high as 7,000,000 to 8,000,000 per c. mm.). High red counts are to be expected in most chronic diabetes.

The *alkalinity of the blood* is materially reduced in the severe cases, particularly before the appearance of acidosis. Excess of fat is frequent; always an unfavorable condition. Digestion leukocytosis is of no prognostic significance. It is frequently present.

Sexual Anomalies.—Periods of sexual weakness, at times *impotence,* may be present during the early stages in men of neurotic habit without grave diabetes, or it may be a symptom in the severer forms of the advanced disease. As a rule with improvement following diet, the sexual appetite returns, though it may not always reach the normal. In the uncontrolled cases in men, sexual weakness may persist. Diabetic women are likely to abort on slight cause—their general condition is usually aggravated by pregnancy, and in the more severe forms there is increase of all symptoms and progression following delivery. I have seen pregnant diabetics die of suddenly arising acidosis. In some women the emaciation has been extreme and rapid. Diabetic women are not likely to become pregnant. *Alimentary glucosuria is present at some time (during varying periods) in* 80 *per cent of pregnant women* (Magnus-Levy).

Infection of the Diabetic.—I have repeatedly in this section referred to the ease with which the diabetic is infected. Among the most frequent infections are *tuberculosis, pneumonia, skin infections* (furuncles), *necrotic foci, pulmonary gangrene* and other minor infections including *laryngitis, bronchitis* and *otitis.* I have separately considered these complications in the chapters dealing with the individual diseases. Syphilis rarely causes diabetes, the association of the disease with the infection is possible and relatively frequent. The general rule may be accepted that *any acute infection with diabetes is serious.*

Pneumonia offers a decidedly unfavorable prognosis, though I have

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had successful issues, among these a severe diabetes in a man 50 years of age.

Tuberculosis with diabetes is uniformly fatal. The diabetic who develops tuberculosis offers but little resistance to the onward march of the infection and seems to "melt away" with prompt breakdown of lung tissue, high fever and rapid heart. In the severe types of diabetes tuberculosis is, next to acidosis (coma), the most frequent cause of death. Febrile, i. e., infectious diseases may occasionally affect glucosuria favorably. This is only true of the milder cases. As a rule following severe infection there is progression in the malignant forms of the disease.

Diabetic gangrene is usually a terminal process dependent upon *endarteritis* (arteriosclerosis) *obliterans,* though occasionally it may limit itself to a superficial patch of skin tissue following infection. The prognosis of diabetic gangrene is unfavorable; it leads to death in coma, in most cases. *Furuncles* are frequent accompaniments of diabetes and may be present at any stage. They are often the first complication to lead to the correct diagnosis. *Diabetic tissue in the advanced stages offers lowered resistance to infection and breaks down with surprising rapidity. Every carbuncle in a diabetic ought to be considered a serious complication.* In the presence of acute or chronic pronounced acidosis it is almost uniformly fatal. Without acidosis a small carbuncle or multiple boils are often controlled. It is often surprising to find how rapid the tissues break down and how certainly coma develops after a few days of mental cloudiness. *Vulnerability of tissues* in diabetes is due to the faulty pabulum received from the surcharged blood. The diabetic should be warned against the possibility of infection from cuts and superficial wounds. The careless cutting of corns in the diabetic subjects has led to frequent malignant infection and death.

Skin Lesions.—The prognosis of superficial skin lesions (infections) must depend upon the associated conditions. In the reduced and in the toxic, furuncles may promptly involve the deeper tissues and lead to death with all of the symptoms of sepsis and acetonemia.

Universal pruritus, or of the *genitals,* may be an early or late complication. When early it usually disappears as the urine is cleared or improves. My experience with severe pruritus has been exceedingly satisfactory in most cases. 21 per cent of diabetics develop pruritus (von Noorden) at some time during the course of the disease.

Nervous System.—The prognosis of diabetes or glucosuria associated with chronic diseases of the nervous system, regardless of the true pathogenesis of the former, is influenced by the extent and nature of the latter. *In alcoholics with polyneuritis* I have met glucosuria which has disappeared with the cure of the neuritis. In my experience the glucosuria with most chronic organic lesions of the nervous system has not been continuous, but has returned from time to time; thus with *brain tumor* sugar may be

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found only occasionally; the same is true of *multiple sclerosis* and *tabes dorsalis* as well as *syphilis of the nervous system. Glucosuria with meningitis* is found in the most serious form of the latter.

Neuritis-polyneuritis.—The peripheral neuritides are frequent, often controlled with great difficulty. In the majority of cases, when an early complication, the pains and other symptoms yield to treatment (diet). When there are peripheral pains in old diabetics, particularly in the extremities, arterial invasion is likely and *gangrene* should be considered among the possibilities. It is safe to promise the majority of diabetics that their pains will disappear as the sugar output and combustion are improved.

Disturbances of the Eye.—There are frequent *ocular infections* in chronic cases; the prognosis of these is usually good. *Diabetic cataract* and *changes in the fundus* (vascular) are frequent and deserve consideration by the specialist. Schmidt-Rimpler mentions the following ocular disturbances in the order of their frequency: cataract, muscular anomalies, retinal changes, amblyopia without discoverable lesion, paralysis of the external and internal eye muscles, iritis, choroiditis and opacities of the lens. von Noorden found retinitis oftener than cataract. Cataract operations in cases of diabetes offer a favorable prognosis.

Disturbances of the Ear.—*Disturbances of the auditory apparatus* are late complications. *Furunculosis of the external auditory canal* in mild cases may be an early complication; in some cases it was fully relieved by diet and prompt local treatment. The otitis of diabetes, when fully developed, is profusely suppurative and there is marked tendency to bone (mastoid) involvement with a fair prognosis following operation.

Gout and Diabetes.—The combination of gout and diabetes mellitus is frequent and as a rule the sugar loss is limited; the patients live during many years but are naturally subject to the accidents of both diseases. Diet exerts a most satisfactory influence in these cases. When gout is advanced and there are visceral lesions (kidney, heart, or arteriosclerosis) the addition of the severe form of diabetes may promptly lead to marked loss of flesh and asthenia. Death due to *angina pectoris, cardiac asthenia, pulmonary edema,* or *cerebral apoplexy,* has been the fate of some of our cases.

Diabetes and Surgery

The clinician is frequently forced to decide upon the feasibility of a surgical operation in the diabetic subject. It is often exceedingly difficult to decide in the presence of a surgical complication whether the *glucosuria* is permanent or simply transitory.

Surgical lesions may cause glucosuria. Smith and Durham have reported cases in which glucosuria disappeared after the removal of sloughing malignant growths. Sugar may appear after surgical operations.

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Phillips showed in his analysis that of 16 cases of malignant disease of the mouth and face in diabetics operated, 11 recovered—or 68.75 per cent—and 31.25 per cent died. "Of purely mouth and lip cases, 9 out of 12—or 75 per cent—recovered" (Risley). Risley reports operations on the breast of 15 cases; 13—or 86.6 per cent—recovered, and 13.4 per cent died. The fatalities were generally due to sepsis and erysipelas. Of 24 operations on the female generative organs, 23 patients gave 5 deaths. Operations on the male generative organs gave a mortality of 50 per cent.

Following fractures, Smith and Durham report numerous cases of "perfect union." Phillips believes that "considerable doubt should be expressed that non-union is more common." von Noorden recommended the use of lime carbonate because of its decrease in diabetic blood for all fractures. I have already considered gangrene, as a complication (See Gangrene). Phillips found that all cases with albuminuria died, and agrees that with acetonemia and an increase in the amount of *ammonia excreted* the prognosis is bad.

Preliminary treatment often improves the reparative processes of the diabetic. Sugar increases the pus producing ability of infectious agents but diminishes their virulence. Phillips' percentage of recoveries was 72.28—a mortality of 27.72 per cent in the entire material he gathered. Risley concludes that "glucosuria should not deter the surgeon from performing any operation of emergency." "Other cases should not be operated in which acetone, diacetic acid, and ammonia cannot be reduced by preliminary treatment." "A mortality of 20 to 30 per cent is to be expected in this class of cases." "This total amount of ammonia must always be estimated. No operation except of the extremest emergency should be performed if there is one gram of ammonia excreted in 24 hours, until this has been reduced to the normal amount—.75 gm." "Operation should be postponed when there is acetone or diacetic acid, even if the ammonia is normal." "Much albumin in the urine is a contraindication to operation and even in small amounts is of bad prognostic import."

The clinician in his treatment of all diabetics should remember that in spite of all statistical reports there is in the individual diabetic increased vulnerability of tissues and in severe cases the danger of coma after all operations needs to be considered.

The profession is in full accord with Tyson who holds that *"diabetes is a disease in which the expectant plan of treatment is disastrous. It is a disease which never gets well of itself and always gets worse if not properly treated."* A patient with diabetes continually stands on the edge of a precipice, he is between rocks, and it is exceedingly difficult to tell when he is to be wrecked.

The patient can do much to increase cellular resistance in cases which do not show malignant tendencies from the beginning, thus preventing the dreaded added infections which kill so many and the intoxications (acido-

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sis, etc.) which end the lives of many more. Underlying all prognostic rules must be placed the one which cannot be controverted, i. e., *the future of the diabetic must largely depend upon his ability to tolerate carbohydrates, as demonstrated by urine analysis and the determination of the sugar content of the blood.*

Joslin believes that the fasting method of treating diabetes is a decided advance in the treatment of the disease, and that the advance has been greater during the past year than ever before. Allen's recent observations are under consideration.

The secondary manifestations may be largely prevented or postponed in the majority of diabetics, for in the final analysis of my material I find that the mild cases are in the majority.

No diabetic can truthfully be told that he is cured; his symptoms only are controlled; once truly diabetic there is no assurance from past clinical experience that the patient does not always remain diabetic, though he may be "sugar-free" during long periods, and finally die of other disease.

There are so many factors which influence the outcome that the individual case must give the data upon which the safest prognosis is based and this can usually be given with considerable certainty when the patient is thoroughly guarded and controlled. In no other disease depending upon metabolic fault are we able to accomplish so much to compensate for existing anomalies as in diabetes mellitus provided the patient is earnest and willing to subscribe to the regimen indicated.

"Eternal vigilance" must be the slogan if the prognosis of diabetes mellitus is to be influenced favorably. "Diabetes is not of necessity a fatal malady. It is the metabolic derangement which proves fatal to most diabetics, hence the efficacy of restricted diet, which is a symptomatic therapy, which has ameliorated the lot and prolonged the lives of many sufferers from diabetes" (Garrod).

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3. *Diabetes insipidus*

Characteristic Features.—The characteristic features of *diabetes insipidus* are *marked and persistent polyuria, low specific gravity urine, and great thirst.* The true nature of the disease is unknown, it is always chronic. Possibly we are in error when we dignify the symptom complex as a disease *per se;* there is no proof of its being a clinical entity.

Dietrich Gerhardt believes that there is an *idiopathic diabetes insipidus* and that it depends upon a *functional disturbance of the kidney.* E. Meyer claims to have demonstrated by functional tests the correctness of Gerhardt's contentions (See original articles; also Umber).

Cases in which the functional tests recommended by Gerhardt, Meyer and Umber fail to localize the cause we look to the central nervous system for the pathologic factor (*secondary diabetes insipidus*).

We do know that in some *insanities, hypochondriasis, paranoia,* and *after concussion of the brain, polyuria,* and inordinate thirst are prominent symptoms; and further we know that polyuria without sugar can be

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produced experimentally by puncture of the floor of the fourth ventricle near the origin of the auditory nerve, in front of the point which when punctured (between the auditory and the vagus nuclei) causes glycosuria to follow.

Experimentally and clinically there are data which tend very strongly to establish the influence of the *hypophysis* in the production of polyuria, great thirst, and all of the symptoms of the disease (Magnus, Schafer, Frank, Oppenheim and Simmonds). *Brain tumors* of specific origin have produced the symptom complex (Nonne). I have seen the complex follow acute infections, but in my material, syphilis has been the leading attendant. Contrary to Umber's experience I have not been able to control the complex in those cases by specific treatment. Umber gives a good prognosis in cases which seem to rest on a syphilitic fundament.

Weil reports families in which the disease persisted during several generations. He reports one family through five generations in which among 220 there were 35 with diabetes insipidus. Among some of these the disease commenced in nursing babes and continued to old age. The oldest of Weil's cases lived to be 92, 87, and 83 years of age respectively.

My cases have shown no hereditary influence. In 6,700 patients (internal diseases) I have had but 4 of the disease. The complex may affect any age. It is three times more frequent in women than in men in England; in Germany Umber found it oftener in men, and the larger number between 15 and 35 years of age.

The quantity of urine secreted may reach between 8 and 10 pounds in 24 hours. There are cases in which 43 pounds were voided (Trousseau). The specific gravity averages between 1,000 and 1,002. In almost all cases the bladder finally becomes tolerant and distended. In some cases the thirst may be somewhat relieved by withholding from 1,500 to 2,500 c.c. of fluid during 24 hours. If the withholding of water is too great patients may suffer excessively and fall into a condition which resembles uremic poisoning; then there is marked unrest, insomnia, delirium, and with severe headache there is likely to be alarming tachycardia. This picture changes with the drinking of sufficient water to quench the inordinate thirst. There are exceptions to this rule; the symptoms of irritability may at times continue several days and become threatening. The *blood picture* in the average case is not markedly changed except when fluid has been withdrawn during sufficient time to aggravate the cardinal symptoms; the blood then shows abnormal concentration and high specific gravity (polycythemia).

The heart and blood pressure are not usually disturbed, neither does the disease in the average case lead to demonstrable change of normal metabolism. The urine remains sugar free unless there is organic central disease (in which localization makes such a combination possible), or there are, as Naunyn holds, two separate processes independent of each

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other (See Senator-Naunyn, Heiberg and Umber). One of my cases had persistent and uncontrollable *backache.*

We are unable to make any favorable impression on these cases by treatment. In cases which seem to justify the surmise that the complex is *primary* and of renal-functional origin, the general health remains unaffected as suggested during years, though the thirst and polyuria make the patients wretched.

Symptomatic cases attending organic disease or injury to the nervous system offer prognosis in accordance with the nature of the cause. There are occasional cases, which because of extreme muscular exhaustion, become bedridden; they usually die of intercurrent disease. Specific cases unless associated with focal symptoms have not in my experience been influenced by treatment.

Conclusion.—*Diabetes insipidus is an incurable complex though it rarely directly destroys life.*

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4. Obesity

(*Fettleibigkeit*)

Causes.—Obesity, or the abnormal and excessive deposit of fat in the body, is due to faulty metabolism, probably dependent upon perversions or the changed reciprocal relations of one or more of the internal secretions (hypophysis). There is not only an abnormal, usually insufficient oxidation of ingested foods, but there may be incomplete combustion with the excessive absorption of foods which make fat. The condition may be either *hereditary* or *acquired.*

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Hereditary Obesity.—There are those who by heredity are disposed to be obese, who in spite of cautious diet and right living are unable to control the excessive deposit of fat. In over 36 per cent of all cases heredity is the leading factor. Such subjects present a hopeless prognosis so far as the marked and continued reduction of weight is concerned, though their general condition may not be materially affected during long periods. They offer, as do all the obese, lowered resistance to acute disease and show tendency very often, as they reach middle life, to degenerative changes.

It has been noted that with the hereditary tendency to metabolic faults, different members of the same family are differently affected—thus one may develop obesity, another gout and obesity, another gout alone, while in the same family gout, obesity and diabetes may exist together or alone or there may be several members who are only obese. Unquestionably the development and prognosis of these conditions in the presence of a strong heredity are enormously influenced by the habits (diet, exercise, etc.) of the individual. In some families no method of treatment will in any way prevent abnormal fat deposit in its female members at the *menopause* and in some at *puberty,* and during one or two years after the development of menstruation there is an enormous fat deposit which in many cases yields; the development of the girl is uninfluenced by the period of obesity. I have seen a number of these girls in whom the improvement was striking and rather sudden. Those in whom there is an inherent tendency to abnormal fat deposit may occasionally find it possible to prevent the condition by close attention to diet and exercise.

Acquired Obesity.—The acquired obesities are dependent upon a variety of causes—unquestionably the leading factors are *faulty diet, insufficient exercise,* and *disease.* The influence of diet in these cases is paramount; when excessive intake and faulty digestion are coupled with *sedentary habits* obesity is invited, and it offers a favorable prognosis only when the underlying faults are corrected. This means scientific treatment and the coöperation of the patient. In the obese *sedentary habits,* as already suggested, invite fat deposit in many subjects while the overexercise of some of these obese subjects, particularly those in whom there is at the same time *fatty degeneration of the myocardium,* may lead to serious cardiac insufficiency—often *sudden death.* The obese subject, whether fat because of his heredity or with obesity acquired, who continues "his rich and unstinted diet," as well as the inordinate use of alcoholics (beer particularly) who with all else fails to take the needed exercise or lives in an atmosphere which is unfavorable to the normal process of oxidation, cannot hope to be relieved.

Anemic subjects are prone to develop obesity, or they may hold an abnormal fat deposit without increase.

Unquestionably the relief of *sexual anomalies* has a favorable influence

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on obesity which may be considered symptomatic. Abnormal fat deposit which develops at the menopause is likely to continue.

"Constitutional inclination" is, according to Ebstein, a congenital disposition to corpulency which can be confirmed by daily experience and proves an enormous factor in prognosis. The "constitutionally inclined" are influenced with great difficulty, and it is not easy to explain the increase of fat in spite of rational diet, exercise and exemplary living in all respects. In considering the prognosis of the *acute infections*—particularly *typhoid fever* and *pneumococcus*—I have called attention to the handicap of the obese. The prognosis of all acute infections is more unfavorable in the fat. Sir James Paget has also clearly insisted, as have the best authorities through all the ages, that "after the age of forty years persons either diverge into spareness or become more or less obese; the former, as a rule, enjoy the happier and longer lease of life."

There are men, who are well developed muscularly, and who after the thirty-fifth year—often near forty—become moderately obese, who are able to continue at their work and often walk without discomfort. This does not apply to men after fifty who become obese, for they do not bear the fat accumulation well. After middle life, in those cases without hereditary burden, under favorable conditions, the fat is absorbed and the associated disturbances are likely to disappear. As a rule it will be found that the prognosis is far better in acquried obesity than in the hereditary cases. Naturally there are exceptions. Laziness and the phlegmatic habit increase all of the ills of the obese; unless these individuals can be aroused, advancing secondary changes make the outlook grave in many cases. Gout in diabetic subjects with abnormal corpulence is considered in the chapters on gout and diabetes (See Diabetes in the Obese), as are also cases with arterial and myocardial changes.

Dyce Duckworth has wisely said what interests us enormously for the prognosis of many cases: "It is not sufficiently recognized that fat deposits are constantly undergoing change by decomposition and reformation. As with all other tissues, intimate change proceeds even in the densest layers of fat; and in no part of the body does any fatty deposit lie out of the current of life and unaltered."

In considering the prognosis of *myocardial disease* I call attention to the association of the *fatty heart with obesity,* also the dangers of *heart weakness due to insufficient exercise* (See Myocardial Disease—Section III, E, 3 (a) and 7).

The dangers of corpulence and inconveniences include besides *depressing mental pang* in many, continuous tax on the myocardium not only *to carry the extra weight of the body,* but to *propel the blood through compressed infiltrated and degenerated organs.* There is also the *faulty oxidation* which in many is associated with *complicating excretory faults.*

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Each case presents features which make the study of its prognosis possible and reasonably certain.

Complications.—The prognosis of obesity also depends largely upon the *complications.* The most serious of all complications is *myocardial insufficiency.* This is, when extensive, associated with threatening symptoms and is fatal in the end. There are cases in which the insufficiency is not extreme, in which the muscle is not extensively involved, in which there are no attending complications, in which treatment (Oertel, Schott-Nauheim, diet, etc.) leads to improvement and comparative comfort.

The *interference with locomotion, often edema of the ankles early,* later edema of the extremities, makes exercise impossible and hastens, because of the enforced inactivity, the cardiac insufficiency.

Cardiac asthma with myocardial degeneration is often serious, but in a fair number of cases, diet with mechanotherapy and resisted movements, may prolong life.

Emphysema with chronic bronchitis and *insufficient heart muscle* offer a bad prognosis in most cases.

Chronic constipation with hemorrhoids is frequent and the latter often bleed and add to the anemia. In the presence of *cirrhosis of the liver,* a frequent combination in the obese due to alcoholism, the prognosis is serious.

Arteriosclerosis with myocardial change and obesity offers a grave prognosis. *Obesity in beer drinkers* with *chronic interstitial nephritis,* or nephritis from any cause with obesity, is always serious.

The obese often die suddenly; the cause is easily explained when we consider the complications referable to the heart, arterial system and kidney mentioned. An occasional trace of albumin with or without a hyaline cast in an obese subject after fifty without heart involvement demands watching, but is not of necessity serious..

Acute hemorrhagic pancreatis with obesity, particularly with fat emboli, is fatal.

In a surprisingly large number of cases, the control of the deposit and the prevention of complications must depend upon the will power of the patient.

In the *plethoric* with obesity, there is tendency to *hypertrophy of the ventricles,* and with *increasing arterial resistance* there is a stage of *hypertension* with final *arteriosclerosis.* The latter condition may precede the changes mentioned. Such patients promptly have *broken compensation with edema of the lung*—always serious.

I have seen the obese with *angina pectoris* and *myocardial insufficiency.* The prognosis for life with *angina and obesity* is very bad; these patients rarely live long after the first attack, particularly if there is associated nephritis and aortic change. *Once the respiration has become irregular* (Cheyne-Stokes) *the prognosis is exceedingly grave. Cerebral*

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(vascular) *complications* offer a bad prognosis. It is always unfavorable to find hypotension-falling systolic blood pressure in these cases with albuminuria and occasional casts.

In the *asthenic or anemic cases* as the disease advances, *dyspnea* and *increasing pallor with small pulse and edema* of the ankles are warnings which call for great caution in prognosis. The degenerative processes are usually progressive after these symptoms appear. Such patients add to their danger because they are unable to exercise. Duckworth calls attention to the frequency of the anemic type of obesity and the symptoms in women "before full growth of the body is established, namely before the age of twenty-two." *Amenorrhea or scanty menstruation* should be expected in the obese. *Pregnancy* is less frequent in the corpulent than in normal women.

Dropsy once developed with obesity makes the outlook dark; *sudden death* is to be feared.

Obese patients furnish a comparatively large proportion of sudden deaths. In the anemic, *syncope* has been noted; *apoplexy, angina pectoris, rupture of the heart, uremia,* with *diabetes acidosis,* and of late the *unscientific use of thyroid extract,* often in large and long continued doses, have furnished the causes of death.

All life insurance companies refuse to accept obese subjects, and with justice. Statistics prove that the obese, whether the disease is inherited or acquired, are in a class which is unfavorable and life is uncertain because of the lack of resistance and the tendency to degeneration. Obese patients are as a rule unfavorable subjects for *serious surgical operations. Change of occupation* in acquired cases from the sedentary to the active often influences prognosis favorably. The introduction of the animal extracts for the treatment of obesity in children and young adults has influenced some cases favorably, particularly those to whom the pituitary substance has been given. *I accent once more the danger of unscientific dieting and the use of thyroid extract in large doses and without medical supervision. Left to itself, uncontrolled by appropriate treatment early, obesity is likely to advance, become chronic and exceedingly rebellious and it unquestionably tends to shorten life.*

The cases of *dystrophia adiposo-genitalia due to faulty function or organic disease of the hypophysis* offers a clear clinical picture of the eunuch type, with enormous fat deposit, particularly over the hips, the breasts and the mons veneris. In these cases the genitals are underdeveloped (hypoplasia) and finally symptoms of *tumor of the hypophysis* may be added—including pressure, headache, increased intraspinal pressure, bitemporal hemianopsia, increasing amaurosis and final choked disk (Umber).

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5. Rachitis

(*Rickets, Englische Krankheit*)

Causes.—Rickets is a disease of infancy due to disturbed nutrition of the body in which the greater changes are found in the bones, though the skin, muscles, respiratory and digestive organs and the blood building apparatus are usually involved. The disease is usually limited to children between the ages of three months and the fourth year; it is occasionally found in children after the fourth year when it has been characterized as *"rachitis tarda"* or *late rickets.* The disease is easily traced to the poorer classes among whom *faulty ventilation, dingy homes without sunlight,* and *improper nourishment* prove to be the causes which lead to the faulty growth of the bone, the insufficient deposit of the lime salts. In all countries *patent foods,* improperly prepared milk—below the standard—and the failure to supply the proximate principles are responsible for the nutritional faults included in rickets. *There are children who are predisposed to rachitis;* thus, in the same family it has been noted that in twins equally fed one may develop the disease, the other escapes (His).

Heredity is an important factor as is also *hereditary syphilis. Advanced rachitis,* often with marked changes in the *long bones* and *constitutional defects,* may heal spontaneously with but small remnant of deformity or ultimate stunting of growth. Rachitic children are predisposed to gastro-intestinal diseases and are without resistance to these and to the other diseases of early life. They promptly fall after infection and are enormously disposed to all forms of *tuberculosis.*

Course of the Disease.—The *bony changes* include, when the disease is fully developed, enlarged head, thinning of the bones of the cranium (craniotabes), open fontanelles, retarded dentition, poor teeth ready to decay, epiphyseal thickening, bowing of the long bones and knock-knee (genu valgum). Bending of the long bones and "green-stick fracture" on

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injury are frequent. *Deformities of the pelvis* and *spinal curvature* often persist during adult life.

The *"rosary"*—prominence at the costochondral articulations of the ribs—usually yields with the other bony changes in the majority of properly treated children. With persistent *improper respiration* the abdomen is prominent, the lungs are insufficiently filled with air, oxygenation of the blood is faulty, and the general condition of the infant suffers. In these cases the "Harrison sulcus" is found (a transverse depression at the level of the ensiform cartilage). The lime salts in the bones are reduced to less than 50 per cent of their normal content. The excessive *sweating of the head* is an usual symptom but does not brand the case as being severe.

The *tardiness of walking* of rachitic children does not affect the prognosis unfavorably, neither does tardy dentition argue against complete recovery.

Hutchinsonian teeth in rachitic children are frequent because many are luetic. Thorough treatment of these leads to very satisfactory results. The flabby musculature may be improved to normal by persistence, proper diet, exercises and healthy environment. The slight *leukocytosis* and *chlorosis* of rachitis yields to treatment, with the disappearance of the other symptoms.

The *enlarged spleen and liver,* often displaced by existing deformities, disappear as time is given for general improvement, and metabolism becomes normal. *All symptoms and skeletal changes may be increased and may become permanent under a long continued starchy and other faulty diet.*

Cases may be considered severe in which there are repeated *laryngismus stridulus, tetany, convulsions* and *motor excitability* (facial spasm). In rachitic children *all infections are more serious than in the normal, and ordinary catarrhal conditions of the respiratory organs demand cautious treatment to prevenet bronchopneumonia and other complications.* This is particularly true of the *bronchitis of whooping-cough, measles,* etc. In neglected cases the *chondrodystrophies* may lead to *permanent deformities.*

The natural tendency of rickets is to recovery, and the evident and palpable deformities, the constitutional disturbances, the faulty respiration, the anemia, the dental decay and the many other symptoms referable to the internal organs, including changes in the spleen, liver and blood may be expected to give way to normal conditions under rational regime. *Permanent deformity of the pelvis and thorax* is not frequent when we consider the large number of rachitic children. *With increasing intelligence and the dissemination of knowledge among the masses, rickets is decreasing and infant life is made more comfortable, while deformities are correspondingly reduced.*

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In rare cases there is a rapid progression—an *acute course* which leads to death within a few months. These cases are associated with rapid bone changes, respiratory, and profound nervous symptoms.

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6. *Achondroplasia*

(*Fetal Chondrodystrophy, Fetal Cretinism*)

Virchow gave the name of *fetal cretinism* to a condition in which there is a dystrophy of the epiphyseal cartilages secondary to connective tissue invasion from the periosteum; there is a premature union of the epiphysis and the shaft which results in dwarfing with the normal development of the head and thorax. The condition is possibly due to dyspituitarism, is congenital, and is held by Jansen to follow amniotic pressure and is considered by him to be closely related to other congenital malformations. He opposes the pituitary origin of the disease. Osler says: "But it is an argument in favor of some associated disturbances of the pituitary gland that achondroplasics often show precocious sexual development." Most of these infants die during the first few weeks of life; if they live they are dwarfs with normal intelligence and fair resistance.

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7. *Osteomalacia*

(*Mollities ossium*)

The loss of lime salts from the bones of the extremities and trunks during adult life associated with softening and bending are characteristic

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of osteomalacia. The condition is exceedingly rare. In 6,700 cases consecutively examined we have not met a single case. When the disease attacks women during pregnancy it is known as *"puerperal osteomalacia"* and in these cases, each subsequent pregnancy is associated with increasing bending and yielding of bone. It has been held that there is an association of mollities ossium with a changed ovarian secretion. As the disease progresses there is evident yielding and the patient is shorter; the gait is "wobbling" "like walking on eggs" and it is difficult to climb stairs. It has been noticed that the menstrual function is undisturbed, conception, it is held, is made easier and twin pregnancies are surprisingly frequent. These cases are usually met in country districts, in women who are underfed, who have many children and in whom the respite between pregnancies is short. About three-fourths of all cases are met during pregnancy.

Early recognition and rational treatment have led to brilliant results. The disease may be controlled. Some have been successful after oöphorectomy, but without hygienic or dietetic treatment improvement is not likely to follow.

Uncontrolled cases finally fall into helpless conditions; they emaciate, appear cachectic, develop gastro-intestinal symptoms, respiratory embarrassment, and die after a period of marked asthenia, or they develop infections, including pneumonia or bedsores and sepsis.

8. *Scorbutus*

(*Scurvy*)

(a) Adult Scurvy, (b) Infantile Scurvy (Barlow's Disease)

(a) Adult Scurvy

Origin and Association.—Adult scurvy is probably of metabolic origin, and is associated with spongy gums and repeated hemorrhages from the mucous membranes of the body and into the skin, with consecutive anemia.

Causes.—Adult scurvy is caused and increased by *faulty hygiene* and *improper* and *insufficient diet.* It is hastened by mental fatigue and worry as well as excitement. There are clinical facts which create the strong suspicion of infection in some cases. Most scurvies, however, are caused by faulty food and may be relieved by change to a favorable environment where proper nursing is included and a dietary including vegetables and fruit acids with sufficient sodium chlorid. The scurvy which has followed long cruises at sea on vessels insufficiently provisioned has in the past claimed many victims. With our knowledge of dietetics scurvy has been prevented, and it is exceedingly rare to meet it on the

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ocean at the present time. Osler holds that it is not a rare disease in the United States. In Central New York we rarely see a case save in tramps, who, neglected and filthy, usually vermin-covered, present at our hospital for admission with large skin hemorrhages, they are thoroughly depleted.

When the disease is *endemic*, as it occasionally is in camps, there is besides filth, faulty feeding. Attention to detail and diet promptly brings relief and while convalescence is often slow, if there are no organic lesions complicating, recovery is the rule. There are occasional cases which are *malignant* from the beginning, in which there are infarcts, and at times the suspicion of *infection and malignant endocarditis;* these offer a very grave prognosis.

Symptoms and Infections.—*Ulcerative gingivitis* with bleeding from the gums is evidence of severe scurvy. *Delirium* and other *meningeal symptoms* increasing to *coma* are found in the severe cases which create the suspicion of infection.

Bleeding from the kidney or bladder is not *per se* serious—most of these cases recover. Profound evidences of *toxemia* with deep and superficial hemorrhages may lead to the appearance of graver disease and yet the prognosis is not of necessity bad. The *pulse* in many cases which end in recovery is rapid, small, and thready and hemic murmurs may persist until the blood picture of secondary anemia has disappeared.

Albuminuria, not dependent upon chronic nephritis, does not influence prognosis unfavorably unless there are other evidences of malignancy; neither does the presence of casts (hyaline) under similar conditions signify danger. *Ocular hemorrhages* usually leave the eye normal.

Cerebral apoplexy may develop, and if it is extensive and into vital centers causes sudden death. *Limited hemorrhagic infarcts* (non-malignant) into the membranes or into the brain tissue do not, as a rule, lead to death. The greater danger from adult scurvy is from the malignant cases and added infection. Death rarely results from simple uncomplicated scurvy.

(b) Infantile Scorbutus

(Barlow's Disease)

Scorbutus during infant life offers an excellent prognosis in the absence of complications. Its recognition and rational treatment is at once followed (almost as if by magic) by improvement and the complete cessation of the usual painful symptoms.

Causes.—Faulty food is *the* cause of infantile scurvy. *Barlow's disease* in the United States is almost always caused by patent baby foods which naturally eliminate from consideration the needs of the individual child, and as a rule fail to meet the demand.

Symptoms.—It is the exception to find breast-fed children scorbutic, though it does occasionally happen. The leading features of Barlow's

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disease include tender epiphyses of the lower extremities, as a rule, particularly at the junction with the shaft (the slightest movement makes the babe cry), subperiosteal hemorrhages causing slight swelling, petechial spots, ecchymoses—conjunctival usually—spongy and bleeding gums, and anemia. There may be considerable weakness and some elevation of temperature. In severe cases intramuscular hemorrhages may continue the tenderness during a considerable period.

The faulty feeding leads to the subperiosteal hemorrhage; the prominent feature of the disease, which is readily overcome, as already suggested by prompt recourse to proper diet and hygiene.

9. *Multiple Myeloma*

(*Kahler's Disease* (1889), *Myelopathic Albumosuria, Bence-Jones Albumosuria* (1848))

Bence-Jones albumose is found in the urine with Kahler's disease, occasionally in grave pneumonia, in purulent processes, and with nephritis (rarely) of specific origin. Albumosuria may be detected by boiling the urine, which gives a white precipitate on the addition of nitric acid, when it disappears to reappear as the urine cools. With multiple myeloma, or Kahler's disease, the prognosis is absolutely bad. The disease is not frequent; I have seen two cases in my series—both died—both gave the Bence-Jones reaction. Christian has fully decided that the myeloma is a veritable neoplasm with cells resembling the plasma "rather than the myelocytes of the bone marrow" (Osler).

Both of my cases were in males beyond middle life; both died within 12 months. In both I was positive that the bone deposit was primary —in neither were there metastases—both were painful. Kahler's original case lived with positive symptoms of multiple myelomata from 1879 until 1887. He was a physician, aged 46, when first seen, and during the eight years of his illness he developed all of the bone changes and deformities characteristic of the disease without lymphatic or splenic involvement. The case was examined post mortem with confirmation of the diagnosis; there were no metastases.

In the diseases above mentioned in which albumosuria is found without multiple myeloma the quantity is infinitesimal. Marked albumosuria, when associated with fragility of the bones or symptoms of *grave anemia,* almost always signifies multiple myelomatous deposit in the bones though the condition may be present during a considerable period before the Bence-Jones bodies show in the urine. Hence, albumosuria with bone symptoms may be considered to be due to advanced multiple myelomata, and the prognosis is uniformly fatal. The *blood picture* is one of grave anemia without features otherwise characteristic. Weber

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makes this unqualified statement: "The presence of Bence-Jones proteid in the urine is practically invariably of fatal significance and nearly always indicates that the patient is suffering from "multiple myeloma," and further, "it is always the result of disease of the bone marrow." "Metastatic tumors in the bone marrow do not give rise to Bence-Jones albumosuria."

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Section X

Diseases of the Ductless Glands

A. Thyroid Diseases

1. Growths
   (a) Tumors—Thyroiditis
   (b) Goiter
2. Hyperthyroidea
   (a) Exophthalmic Goiter
   (b) Myxedema—Cretinism.

1. Growths

(a) *Tumors—Thyroiditis*

Both tumors of the thyroid gland and goiter belong in the domain of the surgeon.

Neoplasms.—The leading neoplasms are *carcinoma, sarcoma* and *adenoma.* In all new growths of the thyroid there is great tendency to metastases. In most thyroid growths there is marked *hyperthyroidea* or *perverted thyroid function.* It is possible, if the patient lives, for the gland "to wear itself out," when hypothyroidea (myxedema) is substituted. The malignant growths give the usual unfavorable prognosis unless primary, detected early and radically treated. Adenoma is amenable to surgical treatment.

Inflammatory Conditions.—THYROIDITIS.—Inflammatory conditions, thyroiditis—*suppurative* or *non-suppurative*—may develop in normal or enlarged thyroids causing swelling, and these may complicate the infections including measles, pyemia, scarlet fever, pneumonia, polyarthritis, tonsillitis, influenza, etc. With these conditions, as with new growths, symptoms of perverted function, hyperthyroidea (usually), or hypothyroidea may develop and in rare cases death may be caused by overpowering and *acute hyperthyroidea.* Naturally the primary infection remains

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the paramount factor in prognosis. Roger and Garnier have called attention to the clinical features of the infections and their dangers.

I have seen a number of cases in which there has been *acute swelling with the thyroiditis* without evident primary infection, but atypical hyperthyroidea and alarming tachycardia, in which life was in danger during several days. A number of such cases have died before the end of the seventh day. The *productive* or *sclerotic thyroiditis* of Riedel is likely to run a rapid course, is associated with symptoms of malignancy and compression. In some cases there has been laryngeal paralysis. This is always a serious condition.

(*b*) *Goiter*

(*Endemic Goiter, Struma, Bronchocele*)

Association.—The relations of the thyroid to vital organs and to the genitals are better understood than ever before, and we are daily accumulating material which justifies the conclusions that any goiter is a swelling which demands close attention, which because of changed function may lead to threatening symptoms without warning, in spite of the fact that *simple parenchymatous goiter in the majority of cases remains without annoying complications.* The close examination of a large material will demonstrate the fact that *many* simple and unsuspected goiters are associated with cardiovascular or other symptoms, that perverted thyroid function is present at some time during the history of most goiters, and that no clinician can offer any forecast which will be of value in deciding whether goiter, in the individual case, will always remain free from the symptoms due to faulty function of the gland. It may be assumed that the patient will be spared the cardinal symptoms now considered due to excessive functional activity but *the presence of a goiter is always significant and its degeneration is possible at any time with all of the accompanying symptoms.*

The *reciprocal relations of the ovaries and thyroid* have been recognized by the lay world and the profession during all the ages.

Frequency.—Simple uncomplicated goiter is increasing in frequency. In 5,370 cases of internal diseases I found 186 goiters—3.46 per cent. Of this number 89, or 1.66 per cent, were simple uncomplicated goiter (Elsner). In France there are supposed to be, according to Baillarger, one-half million goitrous persons. I cannot agree with McHarrison who believes that goiter is less frequent now than formerly. In India there are five million persons with bronchocele.

Distribution.—Goiter is certainly a "place disease"; there are, as may be learned from its close study, *endemic areas* (Alps, Himalayas). In these there may be periods of fluctuation.

Influencing Factors.—*Heredity* is a powerful factor in the develop-

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ment of simple endemic goiter. *Goitrous mothers are likely to beget children with goiter—often myxedematous.*

Persons of *lymphatic and nervous temperament* in goitrous areas are likely to develop the growth and "newcomers to an endemic area are very susceptible to it" (McHarrison).

The infections invite goitrous growth; and gastro-intestinal disease, climatic influences, faulty ventilation, sexual overactivity, pregnancy, fright, long continued worry and repeated emotion—all, in the neurotic, invite thyroid hyperplasia. Contrary to general belief the sexes are about equally affected.

Outlook.—*My experience justifies the belief that the majority of simple goiters recover spontaneously, and this often when there are symptoms suggestive of perverted thyroid function. Return of the growth* after disappearance with or without final hyperthyroidea is relatively frequent. *Spontaneous recovery is held by some to give immunity against recurrence* (McHarrison). The prognosis is materially improved when the patient moves from the goitrous area.

Complications.—It is not uncommon to find *physical signs of heart changes* in the presence of goiter without subjective symptoms. These are the cases in which there is probable *atypical hyperthyroidea* which on slight cause (worry, overwork, sexual excess and other excitement) promptly develop three or more of the cardinal symptoms of exophthalmic goiter. Goiter with symptoms is likely to show some *anemia,* though in most cases it is not extreme; unless complications are superadded, no serious complication need be feared from the blood.

Association with Soil and Water.—In goiter areas, there is a possible *infectious origin,* the *water* and the *soil* are strongly suspected as being the vehicles of transportation. McHarrison, Berard and Gaylord and March have, by experiment, demonstrated the association of soil and water with goiter.

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2. Hyperthyroidea

(Moebius)

(a) *Exophthalmic Goiter*

[*Parry's Disease* (1825), *Graves Disease* (1835), *Basedow's Disease* (1840), *Basedowoid Disease* (*formes Frustes-Stern*) (1908)]

Symptoms.—*Typical exophthalmic goiter includes a complex with four leading symptoms—tachycardia, goiter, prominent eyes* and *tremor. Perverted, deranged or excessive thyroid secretion leads to a complex of symptoms of which tachycardia is the most prominent; the others may or may not be present; they are enlarged thyroid gland, abnormally prominent eyes, tremor, increased tissue waste and mononucleosis.* ' Our increased knowledge of the physiologic effects of thyroid administration and anomalous thyroid function have made recognition easy and have thus enormously increased the number of recorded cases of atypical exophthalmic goiter and have also proved its increasing frequency.

For purposes of prognosis it is important to clearly recognize (1) the minimum of symptoms which justify the diagnosis of exophthalmic goiter and (2) to establish the separate clinical forms of the disease.

(1) **Minimum Symptoms.**—Such knowledge is necessary because we know that *hyperthyroidea may exist without all of the cardinal symptoms mentioned in the definition* at the head of the chapter, indeed but one symptom (tachycardia) persisting without goiter but with the neuropathic habit, may justify the strong suspicion of perverted thyroid function. The *cardiovascular symptoms* are always the most prominent in the clinical history, and the diagnosis may be made without any of the other cardinal symptoms, but with added *mononucleosis, occasional psychic disturbances* or *cephalalgia.*

Associated with tachycardia in the atypical cases which I hold to be the most frequent of all hyperthyroideas, are symptoms referable to the sympathetic system (paralysis or irritation of the cervical sympathetic—Eppinger and Hess), including excessive sweating, moist skin with characteristic ocular manifestations, either the Graeffe, Stellwag or Moebius symptoms—usually the first of these. The diagnosis may be firmly established with tachycardia and one or two ocular symptoms. Such cases include the "*goiter heart*" and the Graeffe symptom alone, or the Stellwag also.

With tremor and a single ocular symptom, the suspicion of faulty function is justified. Periods of improvement in such cases may tend to upset the diagnosis but soon the cardiovascular symptoms are in the foreground and the true condition is recognized. There are cases in which the goiter is not a constant accompaniment of the disease but with an acute exacerbation, *goiter, either one-sided or double, becomes noticeable*

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and abnormally tense; all subjective symptoms increase and during varying periods the complex includes most of the cardinal features.

So varied are the clinical features of the anomalous types of faulty thyroid function that it is occasionally exceedingly difficult without thorough investigation into the previous history of the patient to clear the horizon. Thorough vigilance will lead to conclusions that prove the protean character of the disease. In this connection I would once more emphasize the frequent development of positive hyperthyroidea from the *degeneration of supposedly innocent small or large chronic goiters.* Not infrequently the small, one-sided goiter may be associated with more prominent symptoms than are found with the larger growths—there is no rule to guide the clinician. It must be remembered that acute exacerbations in slightly but previously changed thyroids may promptly cause symptoms and these may subside within limited periods.

Typical and atypical types of the disease by their symptomatology and course, prove that the fundamental fault in both is the same, that in the typical, the *toxemia* is deeper and the increased metabolism definite and striking. *The larger number of tachycardias in women which cannot be explained, whether associated with thyroid enlargement or not, are due to perverted thyroid function.*

My material analyzed at the end of 1913 included 5,370 cases of internal disease among which I found 186 of goiter (3.46 per cent). Of this number 89 (1.66 per cent) were simple uncomplicated goiter; 97 (1.8 per cent) were diagnosticated as belonging to the class of exophthalmic goiter. Of this number 55 (1.2 per cent) of the total number of cases proved to be atypical exophthalmic goiter; 42 (.78 per cent) were typical in all symptoms. These statistics prove that over 50 per cent of all exophthalmic goiters are atypical, i. e., they may be recognized without the presence of all of the cardinal symptoms of the typical type of the disease.

(2) **Clinical Forms.**—The second important factor for prognosis is the recognition in the individual case of the leading features which justify classification. Sattler's statement receives corroboration from all clinicians; he says, "There are types rich in symptoms and even at the height of the disease types poor in symptoms."

I would classify my cases as:

I. Typical exophthalmic goiter
   (a) Acute exophthalmic goiter
   (b) Chronic exophthalmic goiter
II. Atypical exophthalmic goiter
   Basedowoid—formes Frustes (Stern).

The former (I) are those which include in their symptomatology four or five cardinal symptoms of the disease; the (II) atypical types include

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those cases in which one or more cardinal symptoms of the disease are absent during varying periods and in which they may never appear. In all of these cases the dictum of Charcot must be upheld: "Sans tachycardie il n'y a pas de maladie de Basedow." ("Without tachycardia there is no Basedow's disease.")

Heredity.—Heredity plays an important rôle in this disease. It is not at all unusual to find two or more members of the same family with the disease and to note how emotional causes in the predisposed increase a train of previously ill-defined symptoms. The disease selects females by preference and during the period of sexual activity. Acute hyperthyroidea in my material has been more frequent in the male. One male to nine females has been my experience. Buschan in 980 cases of exophthalmic goiter found 175 in men and 805 in women. Leonard Williams makes the unqualified statement that "the greater number of subjects of Graves' disease are degenerates." I cannot entirely subscribe to this statement.

i. Typical Exophthalmic Goiter

(*a*) *Acute exophthalmic goiter*

While the overwhelming number of cases of the disease develop gradually, there are a few in which it suddenly overpowers the patient without warning. My material includes five cases of acute hyperthyroidea; all ended fatally. These latter included one woman, aet. 43, who developed the disease about six weeks after confinement; two were boys aged respectively 12 and 21; one was a man who had an old goiter which had never given rise to symptoms, and one was a girl who out of a clear sky had acute hyperthyroidea with evidences of compression, cyanosis and the cardinal symptoms, and who promptly died.

In none of my cases was there improvement after the initial symptoms; in all there was extreme asthenia, marked cardiac insufficiency, rapid increase in the size of the thyroid, prominent eyes, but not marked exophthalmos; tremor was extreme; there was cyanosis in the terminal stage and glucosuria in two. The temperature was only slightly elevated. Blood pressure was normal until reduced by the terminal myocardial insufficiency.

When acute hyperthyroidea includes severe gastro-intestinal symptoms the loss of flesh and weakness are rapid, the heart becomes insufficient within the first four days, the toxemia causes deep involvement of the sensorium, and death is the rule.

In four of my cases there was *mental torpor* and these were unconscious during the last hours of life. In the males and the young girl there was delirium. The woman, aet. 43, was conscious to the end. I have seen none of the cases described by others (Sattler) in which after an

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acute period the symptoms subsided completely without recurrence. Of the five cases of acute exophthalmic goiter above mentioned only two are included in the 186 cases of goiter, the others were met before the beginning of the series here included.

Manipulation of a goiter, compression for treatment, may promptly produce all of the cardinal symptoms of acute hyperthyroidea and death. One such case I recently saw in consultation (the young man, aet. 21, above mentioned) who had a small goiter for which manipulation was used. His acute hyperthyroidea followed the second treatment and he died before the end of the seventh day. Similar cases have been reported by Briege (vibration treatment).

Acute exophthalmic goiter has followed the use of x-rays to the gland (Cvostek, H. E. Schmidt) and it should not be forgotten that in the presence of goiter alarming or *fatal acute hyperthyroidea may follow the administration of thyroid extract in large doses* (Notthaft) (A. Kocher). That acute hyperthyroidea of mild character may recover there can be no doubt. Cases of *acute iodthyroidism* run a rapid course.

(*b*) *Chronic Exophthalmic Goiter*

(Chronic Typical Hyperthyroidea)

1. *Parry's Disease*
2. *Graves' Disease*
3. *Basedow's Disease.*

The cardinal symptoms of the typical disease are easily recognized—four always leading—the accompanying clinical features are so many that to consider the significance of all would lead us to dilate on most of the organs of the body.

Besides *cardiovascular symptoms, ocular symptoms, including exophthalmos and muscular insufficiencies, goiter, tremor, symptoms referable to the sympathetic system,* the leading clinical manifestations which complicate the disease include:

Spasms—Tic—clonic spasms, tetany, spastic torticollis and convulsive disturbances of the speech
Chorea—(adult and infantile) (A. Jacobi)
Epilepsy—
Paralytic Conditions—Paraplegia, hemiplegia
Myasthenia
Ophthalmoplegia and Bulbar Paralysis
Acute Bulbar Paralysis
Spinal Lesions—Amyotrophic disease; atrophic, anterior disease
Progressive Muscular Paralysis
Multiple Neuritis
Sensory Disturbances

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Reflex Anomalies
Migraine
Insomnia and Somnolence.

OTHER COMPLICATIONS REFERABLE TO THE NERVOUS SYSTEM INCLUDE:

Brain Tumor
Cerebral Hemorrhage
Syringomyelia
Paralysis Agitans
Progressive Paresis
Multiple Cerebrospinal Sclerosis
Locomotor Ataxia
Hysteria
Neurasthenia
Menier's Complex
Psychoses
Vasomotor Disturbances
Digestive Symptoms
Respiratory Symptoms
Diseases of the Genito-urinary Organs
Skin Changes—Urticaria
Pigmentation
Pruritus
Erythema
Purpura
Multiple Fibromata
Edema—localized or general
Dercum's Disease
Myxedema
Glycosuria and Diabetes
Urinary Anomalies—Polyuria
Polydipsia
Albuminuria.

The Prognostic Significance of the Leading Clinical Features.—CARDIOVASCULAR SYMPTOMS.—Tachycardia and other cardiovascular disturbances influence prognosis very materially. Long continued rapid and uncontrolled hearts with gastro-intestinal symptoms and associated emaciation, particularly if there be diarrhea, is a bad and unfavorable complication. The chances for the patient with the "goiter heart" are not bad and it is often surprising to note how erratic and arhythmic the heart may remain during long periods and yet there is final improvement, though not, as a rule, complete recovery. It is further a noteworthy fact that these patients may for years without danger continue at their work, when not too strenuous, without aggravating their heart condition. The prognostic significance of the heart anomalies must be interpreted in connection with the individual case and must include cautious consideration of all the associated conditions. If the myocardium is tired or dilated, without marked degeneration, in spite of abundant blowing systolic sounds and

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arhythmia, the prognosis is not of necessity (for life) bad. Most deaths directly due to hyperthyroidea without complications yield to myocardial degeneration after long periods of uncontrolled tachycardia and dilatation. The persistence of a blowing systolic bruit over the enlarged thyroid is characteristic of true hyperthyroidea and may be associated with "shaking head" with each cardiac impulse (*Musset's phenomenon*).

These symptoms usually yield with the general improvement of the patient. In self-limited cases or in those relieved by surgical operation the heart is often slow to regain its normal balance; it continues irritable, often with relative insufficiencies, dilated, and revolts on slight cause. The majority of these hearts after many months improve and remain serviceable though they may never become absolutely normal. Decompensation is rare unless provoked by carelessness, overwork or added disease (nephritis, arteriosclerosis).

Blood pressure study of exophthalmic goiter, contrary to what might be expected from the small, rapid and often thready and erratic pulse, offers but little of value for prognosis. *Exophthalmic goiter is not a hypotensine disease;* systolic pressure is likely to be normal or little changed during the active period of the disease; at times it is slightly above the normal, rarely hypotensine during the height of symptoms. In the terminal stage or with threatening cardiac insufficiency it may fall far below normal; the associated symptoms at such times offer the indications for safe prognosis.

The pulse amplitude may remain about normal or in the late stages register between 10 to 25 mm. Hg. With hyperthyroidea, glucosuria, arteriosclerosis, and kidney involvement high blood pressure is present and demands interpretation. Such patients properly nursed and rested may live during long periods.

Tremor.—Mild atypical or typical cases are not materially disturbed by tremor. There are but few cases of the complex in which tremor is not present at some time during the course of the disease. There are cases in which tremor is marked, in which it persists uncontrolled by treatment, but it does not *per se* add to the dangers of the disease. Active tremor is very likely to be present with the more profound poisoning and is, therefore, when considered with the other grave and uncontrolled symptoms, of serious import.

Tremor or chorea with deep involvement of the sensorium is always serious and is rarely an accompaniment of the milder types of the disease. Chorea is found occasionally in cases of the disease in early life (Jacobi) and adds to the danger in the presence of endocarditis or pericarditis.

Spasm.—*Painful cramps* are annoying but not serious. Spasms may be tonic or clonic. *Tetany* has complicated one of my cases and was associated with spasm of the glossopharyngeal muscles and threatening asphyxia. In this case there was cyanosis, and it became necessary to

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do an emergency thyroidectomy which saved the life of the patient. In one year, however, there was a return of the same threatening symptoms —*glossopharyngeal spasm, tetany, tic convulsive* and *tachycardia.* In this case, as in most which run a parallel course, the *parathyroids are probably involved.* This complication is exceedingly rare.

Kocher has seen but three cases in his material with tonic spasms. The *Trousseau and Cvostek phenomena* were present in my case and in others reported (Kocher, Mattiesen, Steinlechner, Marinesco, Stumme and Loewenthal and Wiebrecht).

Eye Symptoms.—Exophthalmos or protrusion of the eyeball may be double or one-sided. The atypical cases may escape with but slight exophthalmos; the typical show more or less. *The most serious cases have the more prominent eyes, though this is not a rule without many exceptions.*

Of all the cardinal symptoms of the disease, prominence of the eyes is most frequently absent. In 1,415 cases of Basedow's disease 330 never showed exophthalmos, i. e., 23.2 per cent (Sattler).

Exophthalmos as a single symptom is of little prognostic value; its persistence with other uncontrolled symptoms argues in favor of deep toxemia. It is not always constant, may recede during long or short periods. It is not likely to return alone, but always with one or more of the cardinal symptoms—usually erratic heart (tachycardia). The other vascular symptoms are not indicative of the seriousness of the disease.

Goiter.—Throughout this chapter I have repeatedly referred, in connection with my consideration of the influence of symptoms, to the enlargement of the thyroid gland, and I feel that I have demonstrated the fact that the size of the goiter does not bear close relation to the severity of the symptoms; indeed small insignificant enlargement is often associated with malignancy of symptoms and large masses may do their greatest harm by pressure. Acute increase in the size of the gland is always of significance. The small one-sided goiter may, when its activity is increased, prove a serious menace. My material includes cases in which such a condition frequently threatened the life of a patient whose hyperthyroidea finally yielded without operation, with the result that she has remained well during eight years.

Thymus enlargement is a frequent complication of hyperthyroidea; it may cause serious pressure symptoms or it may lead to sudden "thymus death." It is my belief that in occasional acute cases with suddenly enlarging thyroid and thymus, the latter has been the more important factor in causing death. The thymus is involved in most severe hyperthyroideas.

Repeated attacks of *tonsillitis* have a decidedly unfavorable influence on the disease and tonsillar infection is easily contracted. *Tonsillectomy*

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has in a number of cases prevented repeated infection with associated depression.

Sweating.—*Excessive sweating* has a depressing effect in some cases; as a rule it is not of great prognostic import. It is usually associated with disagreeable "flashes of heat" and erythema, and is more uncomfortable than weakening.

Loss of Weight.—*Faulty metabolism* and *rapid waste* are characteristic of many cases. The *loss of weight* may be enormous during the early period of the disease or with acute exacerbations of chronic hyperthyroidea. *Loss of weight alone* offers but little which justifies prognosis. Without other symptoms of overpowering toxemia it is not of serious import; if, however, *loss of weight* is *associated with marked cardiac asthenia, dilatation, myasthenia and persistent gastro-intestinal symptoms* (vomiting, diarrhea and anorexia) the forecast should be guardedly given. Most of these cases unless promptly controlled end fatally within a limited period.

Mental State.—Patients with marked mental anomalies may improve very materially, but complete return to the former normal state in chronic cases is hardly to be expected. With the psychoses fully developed we have been very unfortunate. Some have been committed to state institutions and have not improved; others have remained at home—chronic psychopaths never materially improved; while others have developed acute manias and have died within a few weeks or months of the development of the psychosis. *Hysteria, hystero-epilepsy* and the emotional element are not easily controlled in the chronic cases. Periods of improvement are often followed by relapse.

The Complications Referable to the Nervous System.—The organic changes of the nervous system mentioned above are not materially influenced by the presence of hyperthyroidea; while the latter is unfavorably influenced by the addition of any one of the graver anomalies of the central or peripheral systems. I have elsewhere in this volume considered the association of *epilepsy with exophthalmic goiter*, a combination which may not end in death directly from the combination, but it offers little or no hope of relief.

Migraine, insomnia and *somnolence* with hyperthyroidea are in most cases amenable to treatment.

Paralytic conditions once present are likely to persist; their prognosis must be based on the associated primary lesion. The addition of *acute bulbar paralysis* is promptly fatal.

Digestive Disturbances.—I have frequently referred to the overpowering influence of digestive disturbances The most unfavorable cases are those in which digestion is impaired beyond repair, in which *colliquative diarrhea* with the typical disease saps the patient's strength.

The Respiratory Symptoms.—These may be due to the toxemia, to

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pressure, to infection or indirectly to heart lesions. Each of these causes demands separate consideration in the individual case.

The Skin Changes.—*Urticaria, pruritus, erythema, edema* (localized and general) may yield after medical or surgical treatment. *Purpuric conditions* are always serious; they should lead to cultural tests when present with symptoms of infection; they may be due to malignant endocarditis, when they end fatally. The pigmentation, fibrosis and trophic disturbances are permanent (see separate chapters—Dercum's Disease, etc.).

Genito-Urinary Organs.—There are but few cases of exophthalmic goiter which in women are not preceded or accompanied by menstrual disturbances. I have shown in an article recently published that *15 per cent of all cases of goiter are associated with uterine myoma or fibromyoma.* In these cases there is a strong hereditary tendency to both goiter and uterine myoma.

A family of seven daughters was found in which a number of aunts and cousins on the father's side had goiter; six of the seven daughters had uterine myomata and four had goiter. The mother was free from myoma or goiter.

Operations for the uterine growths offer a good prognosis; the removal of the goiter does not influence the myoma; the removal of the myoma does not materially influence the goiter, but it often influences the tachycardia favorably. The genito-urinary complications are not usually of serious import. *Transitory albuminuria* is not infrequent. *Nephritis* may prove a serious complication but is not usual.

Typical and severe exophthalmic goiter has been seriously affected by profuse *hematuria* in two of my cases; in both, there was nephritis with probable purpura.

Glucosuria and Diabetes.—I have elsewhere considered the influence of the ductless glands on the liver, sugar production, retention and associated acidosis (See Diabetes Mellitus).

There is a close relation between the thyroid and the pancreas; the secretion of the former materially modifies the function of the latter. The presence of glucose in the urine in hyperthyroidea depends upon a changed relation in all probability of these organs to each other—a fact which is strengthened by our inability to produce glucosuria after thyroidectomy or in myxedema.

With profound *involvement of the adrenals and associated diabetes or glucosuria* weakness becomes extreme, tremor excessive, the cardiovascular symptoms are aggravated, there is rapid tissue waste, and the outlook is bad.

Myxedema.—Exophthalmic goiter with all of its typical symptoms of hyperthyroidea may, when the gland has worn itself out, be displaced by fully developed myxedema and in these cases the hyperthyroidea does

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not as a rule, recur, but the myxedema is favorably influenced by thyroid extract continually administered. Just so soon as it is discontinued, the symptoms recur. My series includes one case. (Moebius reports similar experiences.)

Acromegaly.—When thyroid overactivity is associated with acromegaly, the latter, as in uncomplicated cases, remains uninfluenced by any known treatment. One of our cases of goiter with mild hyperthyroidea developed acromegaly and syringomyelia. The patient is still living after many years of continuous and uninfluenced symptoms though she has since had a hysterectomy and oöphorectomy for fibromyoma of the uterus and ovarian cyst; she also has a ranula, pigmentation of the skin and multiple skin fibromata.

Blood Picture.—In the average advanced case there is a *reduction of erythrocytes; there is leukocytic decrease with monolymphocytic increase, eosinophilic increase, reduction of mast cells. Transitional forms may be either increased, normal or reduced.*

Grawitz offers an unfavorable prognosis in cases in which there is an *absolute lymphocytosis.* Kocher has found, after operation, a fall of lymphocytosis from 48 to 2.7 per cent and a return of neutrophilic leukocytosis. Such results are not surprising and are found after other operations (laparotomies). The consensus of opinion justifies the conclusion that the prognosis of the disease is more unfavorable in cases with marked leukocytosis and high absolute lymphocytosis. Coagulation time is prolonged and autolysis is increased on the addition of the blood serum of the hyperthyroideic patient (Kottmann, Blumenthal).

Kostlivy concluded from his surgical material (already mentioned) that radical intervention was exceedingly grave with absence of mononucleosis (lymphocytosis).

Grave or secondary anemia in all cases adds to the danger; ultimately the outcome must depend upon the cause of the added anemia and the resistance of the patient.

ii. Atypical Exophthalmic Goiter

The preceding pages include the consideration of the prognostic significance of the separate symptoms of hyperthyroidea. In the atypical type of the disease there are, as a rule, fewer grave symptoms and complications; while the course is often chronic, the patient bears the toxemia fairly well and is less likely to fall into the asthenic state characteristic of the grave type.

Atypical exophthalmic goiter may merge into the typical complex without more than a short period of increasing symptoms, or the metamorphosis may be gradual. Close watch will unearth a large number of unsuspected atypical hyperthyroideas in which the cardiovascular symp-

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toms will remain in the ascendency. *It is an established fact that atypical cases are likely to prove chronic, and with one or two symptoms many continue uninfluenced by medical treatment.* The surgical treatment of these cases does not in the majority of cases entirely and permanently relieve the leading subjective complaints.

Stern's *basedowoid disease* deserves to be classified among the atypical hyperthyroideas. In these, the symptoms can be easily traced to early life though the complex remains undeveloped and decades may pass before its leading features are developed. In these cases the trophic disturbances are in the foreground—the typical types of Basedow's disease develop in only 3 per cent before the twentieth (20th) year, while 60 per cent of atypical, or basedowoid, cases are found before that time.

The atypical types develop in those with neuropathic tendencies and marked heredity. The basedowoid cases are less likely to suffer from continuous tachycardia than are the atypical cases which are more closely related to the genuine degenerative types. Tachycardia recurs during acute exacerbations—in paroxysms. The atypical cases of the basedowoid type do not as a rule develop marked exophthalmos, while the Graeffe phenomenon is not constant, the Moebius is frequent, the Stellwag is usually present, the goiter small and soft and the systolic bruit over it absent, tremor is present and choreatic. The heart is arhythmic, not enlarged; often a systolic bruit is heard; respiration is irregular. The reflexes are exaggerated. The basedowoid type is obstinately chronic but its mortality is low. The operative results are not favorable in this class of cases.

Goiter Heart (Kraus)

Atypical Hyperthyroidea

The so-called goiter heart of Kraus in which cardiovascular symptoms are added to a preceding symptomless goiter or a suddenly appearing goiter, is considered among the atypical types of the disease, dependent upon perverted thyroid function or hyperthyroidea, in which the prognosis for life is good but complete relief from tachycardia is hardly to be expected. These patients show "irritable hearts" on slight cause, perspire freely and are likely to show marked tremor. The ocular symptoms are variable but not persistent. These cases may develop the typical complex on comparatively slight cause: after profound shock or emotion, infection, pregnancy, gynecological operations, or the administration of large doses of thyroid extract (Kraus, Barker, Kocher, Ball, Riedel, Wells, Gitterman, Auld, Rogers).

Goiter and Hyperthyroidea

When a goiter (uncomplicated) in an adult has remained unchanged many years and enlarges perceptibly without known cause (pregnancy

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occasionally), hyperthyroidea may be expected to develop and the symptoms are likely to be typical.

There is no time in the history of ordinary goiter when either typical or atypical exophthalmic goiter may not develop. Billings reports 20 years of uncomplicated goiter with final hyperthyroidea. Kocher (A.) reports cases in which exophthalmic goiter developed after from 3 to 12 years of small or large goiters, and Kocher (W.) reports 72 cases of this kind of which 60 were operated without a single fatality. Of 53 cases followed, 51 were permanently cured and two improved.

Relapse in both typical and atypical cases apparently cured is not unusual and attention in offering prognosis should be called to this possibility. Some relapses are mild and evanescent, others are severe, acute, and may promptly lead to death, especially in those who have been weakened by repeated exacerbations. Relapse may follow radical operation for exophthalmic goiter; Kocher believes that in these cases insufficient thyroid was removed. My experience has not always corroborated this conclusion; I have met relapses after both ligation and radical operation.

Thyroid Neoplasm and Hyperthyroidea

Sudden development of symptoms of hyperthyroidea in adenoma or malignant neoplasm of the thyroid is possible and usually leads to progression of both physical and mental weakness, and does not improve.

Nodular masses in the enlarged thyroid are always of serious import, for degenerative change or perversion of function leading to persistent and threatening hyperthyroidea must be expected. There are cases of *goiter with multiple adenoma* in which periods of exacerbation are followed by relief, but in the end particularly in men who continue to overwork, sudden and severe cardiac insufficiency may cause dilatation and death.

Hard thyroids with multiple nodular deposit and erratic heart demand close watching; such combination is serious.

Self-limitation and Spontaneous Cure

In a large number of cases hyperthyroidea proves to be a self-limited process, and approximate cure in the presence of all of the striking symptoms of the disease is by no means infrequent. Spontaneous cure may include the disappearance of exophthalmos and tachycardia as well as tremor.

In these cases added insult—emotional factors—will be likely to provoke short periods of symptoms or recurrence of all symptoms, or there may be but short periods of symptoms during acute exacerbations. Some of the basedowoid cases, a few of the typical chronic cases may to all

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appearances remain perfectly well and die of intercurrent disease. One of my typical cases ran its course to full recovery in two years; she remained well fifteen years, when a myoma uteri which was present early in her history degenerated and she died of cancer of the uterus. Pregnancy influences the disease unfavorably, aggravates it and may cause such alarming acute hyperthyroidea as to threaten life.

The psychic element (*suggestion*) enormously influences hyperthyroidea. There are cases in which, under favorable surroundings with rest and healthy suggestion, the improvement of all symptoms follows promptly. There are a number of recorded cases in which systematic hypnotic suggestion has led to full recovery.

Rest, freedom from care, wholesome living and change of scene are powerful factors and influence prognosis favorably.

Children rarely develop the disease, with them the acute types are usually fatal, though recoveries are recorded without recurrence (Sattler). My series does not include a single case. In dispensary and hospital practice an occasional typical chronic case presents in which the heart lesions are usually advanced.

Leonard Williams in considering the results of the *operative treatment of exophthalmic goiter* has recently said: "The truth is, these operative procedures in Graves' disease represent the heroid application of loose conclusions from insufficient data." He believes that "the production of the symptoms" is not due to the goiter but "the evidence points strongly—even overwhelmingly—in the direction of showing that the thyroid is merely an unwilling agent" . . . "and reflects reluctantly enough a disturbance which originates elsewhere." We do not commend this statement as justified without qualification and amplification but give it to prove that in spite of brilliant results the last word has not been written on the influence of surgical operation for the relief of thyroid anomalies.

Mortality

It is exceedingly difficult, in fact, impossible to give a figure which even approximates the truth concerning the mortality of the disease. There are so many factors to be considered and so many complications which influence the issue that no statistics can be considered reliable. The author can simply offer those which he has and must look to the future for more reliable data. Mortality in my cases has not been high. In central New York we rarely record a death due to uncomplicated hyperthyroidea. Eight per cent is a high figure to offer and it is unquestionably above the average of treated cases in New York State.

Sattler gives his mortality at 11 per cent.

Kocher 22 per cent.

Mackenzie 30 per cent.

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Operated Cases.—Kocher reports 76 per cent cured (with persistence of exophthalmos in one-fourth of these). His mortality was 3.9 per cent; one-third of his cases were repeatedly operated.

Eiselberg's Klinik: in 45 cases there were 3 deaths among the first four operated; in all he had 6 deaths. Eighteen of his patients were permanently cured, 8 improved.

Mayo, Charles H.—1 to 3 per cent mortality following operation.

Tinker, Martin—less than 1 per cent mortality following operation.

Schultze—72 per cent cured, 12 per cent improved, 2 per cent absolute failures or accidents, 12 per cent deaths.

Rehn—75 per cent cured, 9.8 per cent improved.

The ultimate influence on symptoms in Tinker's and Mayo's cases, as I interpret their reports, are possibly more encouraging than are those of the Continental operators.

Capelle reports that 100 per cent of operated cases which ended fatally showed enlarged thymus glands, and Kostlevy holds that in the absence of mononuclear lymphocytosis the prognosis for surgical intervention is exceedingly grave.

There are occasional cases of hyperthyroidea in young subjects (usually males) with large goiter and a remnant of thymus gland which at times cause acute and threatening attacks of asphyxia. These cases are always serious and when massaged the symptoms of hyperthyroidea may be promptly aggravated; the pressure may cause cyanosis, the cardiac asthenia is extreme and death may follow. Such cases justify thyroidectomy even in young subjects; for the prognosis is surprisingly favorable following the operation.

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(b) *Myxedema—Cretinism*

(Thyroid Insufficiency, "Cretinoid Change," Cachexie Pachydermique)

Thyroid Insufficiency.—The abolition of function of the gland or partial or complete reduction of the parenchyma of the thyroid leads to a complex of symptoms which is easily recognized because of characteristic myxedematous infiltration of the subcutaneous connective tissue. There is dry skin, subnormal temperature, mental tardiness, often atrophy of the thyroid gland and marked reduction of vital processes—metabolic

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particularly—reduction of animal heat; trophic changes in the skin are prominent, as are those in the nails, hair and teeth. There is marked tendency to early arteriosclerosis—to infection and death from tuberculosis.

The "*maximal thyroid insufficiency*" is found when there is complete absence of development of the gland or in cases in which the entire structure has been removed surgically (*Operative myxedema*).

Leopold-Levi has recently dilated on the functions of the gland in considering its insufficiency and for purposes of prognosis I quote the following: "The function of the thyroid gland is manifold. It controls the nervous system, the nutritional exchanges and the humoral equilibrium." "There is increasing evidence to show that it is in part responsible for the process which I propose to describe as thermogenic, oregogenic, morphogenic, antigenic and prophylactic."

In the consideration further of the influence of the gland and the dangers of its insufficiency, the clinician should remember that its two main functions include the "promotion of cell growth, and the elimination of the waste material which results from the destruction of the tissues" (Hertoghe). Its disturbance affects the "chemistry of the entire organism" unfavorably. Hypothyroidea reduces the normal resistance to infection and invites blood changes—hemophilia, anemia and lymphocytosis.

The English school has done more than any other to base our knowledge of hypothyroidea upon a solid foundation. In 1873 Sir William Gull called attention to a condition which he termed "*cretinoid change.*" In 1877 Ord spoke of the same condition as *myxedema;* about the same time Charcot noted the complex and named it "*cachexie pachydermique*"; Schiff and George Murray immortalized their names by proving experimentally that *the removal of the gland and its grafting into the animal produced symptoms in direct proportion as they supplied or removed thyroid substance.* The removal or destruction of the gland produces a characteristic *cachexia* which is fatal unless the continuous administration of the thyroid extract or substance compensates for the loss.

In the consideration of thyroid insufficiency I adopt the classification of the Commission of the London Clinical Society:

I. *Operative Myxedema* (cachexia strumipriva)
II. *Sporadic Cretinism* or myxedema of the child
III. *Endemic Cretinism* (ordinary myxedema or myxedema of the adult)
IV. *Cretinoid State* due to complete loss of gland function.

Deficient or reduced thyroid function from whatever causes produces practically parallel symptoms and tissue changes. In *children* it is safe to forecast more or less arrest or inhibition of the normal proc-

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esses of growth and the subcutaneous changes may vary, while in the *adult* there is usually greater infiltration of the skin—face and hands particularly—in proportion to the gland insufficiency. The prognosis is in occasional cases favorably influenced by the compensatory hypertrophy of the gland or accessory thyroid if present.

Hertoghe calls attention to "those fortunate instances in which pregnancy is accompanied by resorption of the infiltrates." . . . "The favorable phenomena in such cases are due to the hypertrophy of the thyroid, by which pregnancy is accompanied." Such patients again lapse into the subthyroid condition after pregnancy or lactation.

i. Operative Myxedema
(*Cachexia strumipriva*)

Total extirpation of the thyroid gland invariably leads to myxedema. When the parathyroids are completely removed at the same time, *tetany* promptly develops and in almost all cases causes death. Operative myxedema will in the future demand little consideration from the surgeon for he has learned the effect of total thyroidectomy and is governed accordingly in his work. Occasionally *malignant growths* demand the total removal of the gland, in which cases the prompt administration of the thyroid extract prevents operative myxedema.

Accessory thyroid tissue after operation may hypertrophy and compensate for the loss of the gland.

In complete removal of the gland it may occasionally cause mild cachexia which is promptly relieved by the organic extract and does not return if its use is continued.

ii. Sporadic Cretinism—Congenital Cretinism—Myxedema of the Child

Congenital cretinism uncontrolled, unrecognized early, will invariably lead to developmental faults, both physical and mental.

The evidences of hypothyroidea appear after the first few months of life. The conditions which are uniformly present in all varieties of myxedema soon follow. Growth is stunted; the mental status at times in severe cases shows the cretin with but few or no human attributes; the skin is dry; the tongue large, thick, heavy, protruding continually with persistent drooling; the eyes are half closed, the face expressionless. All these children look alike and remain oblivious to their surroundings, restless and crying much of the time, often developing hernia. As they grow older it is noted that there is no hairy growth, the teeth usually fail to develop; if they do develop they promptly decay and break. The hands become more and more "spadelike," the eyebrows thin or absent, the lids puffy, the myxedematous tissue persists boggy, more or less resistant.

The untreated cretin who lives, at sixteen years of age is no larger than

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a babe of two years. There is persistent mental torpor; these subjects learn nothing, they grasp nothing and are of the Mongolian type; they are idiotic. Life may be prolonged until thirty-five or forty years in some cases, though the majority die young of intercurrent infection, tuberculosis, pneumonia, etc. I saw one male, aet. 35, a typical cretin without sexual development who resisted a severe pneumonia. Untreated cases are likely to die within the first two years of life. The blood shows anemia, lymphocytosis and eosinophilia. Reaction to pilocarpin is lowered while adrenalin glycosuria is also reduced, but less than in adult myxedema.

Prognosis.—The *inhibition of growth* in all directions persists in all cases of congenital myxedema so long as the condition remains undetected or untreated. *Sporadic cretinism treated early offers a good prognosis.* The marvelous and prompt effect of a few grains of the thyroid extract in these cases is surprising; the introduction of the organic extract for the treatment of this anomaly is at once the greatest advance of modern medicine. The prognosis formerly absolutely bad is now encouraging; it requires only early recognition and persistent treatment to keep these patients comparatively normal. *No myxedematous child or adult, unless there is thyroid growth or the organic extract of the gland is given as is his ordinary food in sufficient doses at stated intervals, can be expected to remain normal. There will always be a tendency to the subthyroid state.* It is surprising to note how small the dosage needs to be to hold the cretin and promote growth.

The congenital cretin who escapes treatment during the first decade of his life may be materially benefited by treatment, but his growth will not become normal; neither will he develop mentally as he would had he been given the food early (organic extract) which the athyroidea or hypothyroidea demanded.

Treatment of the cretin after the tenth year is not encouraging, and the prognosis grows more unfavorable with increasing years and neglect. *Congenital defects*, unfavorable surroundings, faulty feeding and a variety of factors are paramount in the prognosis of these children. The removal to well-appointed institutions where treatment can be systematically followed increases the chances materially.

iii. Endemic Cretinism

(*Ordinary Myxedema—Adult Myxedema*)

Adult myxedema is more frequent in women than in men. The close relation of the thyroid and organs of generation, leading often to exhaustion of the functionating ability of the gland, may account for the greater frequency of the disease in women.

The symptoms develop insidiously, with the changed features and

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characteristic skin changes; there is mental lethargy, including slow and monotonous speech. The mental processes in most cases are accurate but slow; the patients are able to think but thinking is exasperatingly tardy. The thick tongue of the congenital type is almost constant. The untreated cases develop moderate deafness, changes in the vocal organs, and ocular disturbances; besides the usual skin changes there are sluggish circulation and subnormal temperature. There is often reduced electric excitability of the pneumogastric and sympathetic. *Early arteriosclerosis* in this form of hypothyroidea is an annoying and serious complication. Uncontrolled myxedema in the adult leads to *intestinal paralysis—chronic constipation.*

Blood changes are the same as in the infantile form of the disease. *Myxedematous anemia and blood changes* are favorably influenced by thyroid administration as are also the metabolic processes which without such treatment remain subnormal.

Myxedematous adults show a high tolerance for grape sugar while the ability to cause *adrenalin glycosuria* is also reduced. Severe cases may show genital anomalies—amenorrhea, sexual weakness.

Hypophyseal lesions are not uncommon and unfavorably influence prognosis.

Prognosis.—Myxedema may develop in the adult after a period of exophthalmic goiter, and offers a favorable prognosis (See Exophthalmic Goiter). In the absence of complications the prognosis of adult myxedema is good under rational organotherapy. *Advanced arteriosclerosis and added infection, tuberculosis, pneumonia, myocardial disease* and *nephritis* naturally deserve consideration in the individual cases and influence prognosis unfavorably.

The use of the x-ray for diagnostic and prognostic purposes in all forms of myxedema offers valuable data; bone growth, hypophyseal involvement and other processes may be thus followed.

iv. Cretinoid State Due to Complete Loss of Gland Function

Probably in most cases of cretinoid degeneration there is some remnant of thyroid function. The cretinoid degenerate is found oftener in Switzerland (Central Alps), Carpathia, in the Pyrenees and in the middle mountainous regions of Germany, than anywhere else. Unquestionably infected or tainted water holds the pathogenic toxin. These unfortunates are poorly housed, most are dwarfs, mentally dull, sexually undeveloped, and inefficient with goiters of varying size—"Degenerative histologically" (Falta).

To these cases only the earliest recognition and treatment offer hope of any improvement. The majority live on aimlessly, develop cardiovascular lesions, tense arteries and infections.

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Heredity.—In all forms of myxedema *heredity* is an important factor in etiology. Syphilis and tuberculosis, gout or diabetes and syphilis or tuberculosis, alcoholism and syphilis are paramount, for as Hertoghe has taught, "true congenital myxedema is the outcome of the superposition of two grave blemishes in the parent."

Prognosis.—*It may be assumed that the average subject of myxedema —whether congenital or acquired—always remains myxedematous so long as the gland structure fails to functionate or the absence of thyroid secretion is not compensated by the administration of the organic extract. The prognosis of all forms of myxedema is therefore good so far as life is concerned, and will, as already suggested, continue favorable with thyroid administration in the absence of complication.*

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B. Diseases of the Pituitary Gland

(*Dyspituitarism*)

1. Hypopituitarism

Infantilism

The subject of infantilism never lifts himself above the physical and mental status of childhood. There is faulty or no sexual development in the majority of cases. There is in all direction an inferiority, a lack of the normal ability to produce or serve, or even an approach to the lowest ordinary mental or physical standard.

Cause.—Probably we shall ultimately find that whether *general* or

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partial, infantilism is primarily due to some faulty internal secretion, *hypopituitarism*. Even in those cases in which long-continued disease early in life has led to the *cachectic type*, it may be assumed that the faulty development is consecutive to changed relations of one or more ductless glands or direct change in histologic build and consecutive perverted function of the pituitary gland. *Cachetic types of infantilism* are found in hereditary syphilis, the tuberculous, the offspring of morphinists and alcoholics.

Types.—Freund and von den Velden have recently classified all infantilism as either

(a) General
(b) Partial.

(a) General Infantilism may be an accompaniment of myxedema —cretinism, monogolism, absence of or miniature genital organs; it may accompany suprarenal, thymus or pancreatic disease. Syphilis, alcoholism, lead or mercurial poisons or morphinism in either parent, tuberculosis, chlorosis, congenital heart anomalies, pellagra, faulty hygienic surroundings or underfeeding may lead to infantilism in the offspring.

(b) Partial Infantilism includes:

Infantilism with abnormally small and undeveloped sexual organs, cardiovascular congenital faults.

Infantilism with faulty vocal organs—high-pitched speech, with faulty growth of hair (face and pubes) or with the mental attributes of the infant, during life (Freund, and von den Velden).

Cretinoid infantilism may show some improvement when early detected, when sexual organs are present and complete and when treated with thyroid substance (See Myxedema and Cretinism). *Those cases of the Fröhlich type* (*dystrophia adiposo-genitalis*) are not influenced by treatment; they are obese, awkward, with genitals undeveloped. In these cases there are positive evidences of pituitary disturbance (dyspituitarism of Cushing).

Marburg has divided the cases of *general adiposity* and *underdeveloped genitals* into (1) simple adiposity, (2) adiposity with genital atrophy and (3) simple genital atrophy; and Church adds a (4) type of infantilism in which there is a lack of physical and sexual growth. Marburg insists that hyperfunction of the pituitary ends in acromegaly, that hypopituitarism or hypofunction causes general adiposity and genital dystrophy while entire destruction or defect or complete loss of function produces a *cachectic condition* much like cachexia strumipriva.

The subjects of infantilism may show all of the features of *continuous youth* (ateliosis), or wrinkled and inferior they present the picture of *premature old age* (progeria). Gilford has called attention to these two types. The ateliotic cases are either *asexual* or *sexual*. The *asexual type*

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is more a developmental fault than cretinoid or specific, while in the *sexual form* the development of the sexual organs begins at puberty and the body remains dwarfed (Tom Thumb type).

Outlook.—*All subjects of infantilism, whatever the type, always remain inferior*, ready to yield to traumatism, particularly liable to injury of the genitalia, subject to infection and without resistance. The cell resistance is never normal and complete recovery from diseases, constitutional or infectious, is not to be expected. There is never a moment when the subject is not to be considered pathologic. The daily tax, as Freund has well said, cannot be met and tuberculous infection finds a ready habitat in the lungs and other organs of these subjects. There is no treatment which favorably or permanently influences the mental or physical status of these unfortunates, though some cases have been reported improved by pituitary administration. The majority die young.

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2. Hyperpituitarism

Acromegaly

(Pierre Marie, 1886)

Diagnostic Factors.—In the consideration of acromegaly the reader is reminded of the facts upon which we base our modern conception of the disease. In abstract they are the following: The pituitary body consists of three parts:

(a) The anterior lobe or glandular portion
(b) The middle portion
(c) The posterior lobe or nervous portion.

In true acromegaly the change is probably limited at first to the anterior or glandular lobe and the pathologic lesion is, as a rule, the growth of adenomatous tissue—true *adenoma*. The anterior lobe performs an important function in its relation to body growth, more particularly the osseous system, and there seems further to be a strong relation between this lobe and the sexual organs.

The intermediate or middle portion is not related to skeletal growth

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but exercises an important function in keeping up blood pressure, slowing the heart, "increasing the activity of smooth muscles and causing increased secretion of the urine, the gastric juice and the milk" (Vincent). This lobe also exerts an important influence over carbohydrate metabolism. Vincent and others hold that the secretions of the middle lobe are passed on into the "nervous" portion proper (posterior lobe) where they become converted into more active forms, or become concentrated.

Association.—I have, in other chapters, called attention to probable reciprocal relations of the ductless glands and to the frequent association of lesions in two or more at the same time and compensatory changes after removal of one ductless gland. The hypertrophy of the pituitary body after thyroidectomy is an example. Diabetes is frequent with dyspituitarism, which as the disease progresses, often yields and surprising tolerance for sugar develops (See Diabetes Mellitus, also Exophthalmic Goiter). *Goiter and acromegaly* are comparatively frequent in the same subject; in one of my cases goiter, acromegaly and syringomyelia were found with a number of other lesions (Elsner).

Importance of Pituitary Gland.—The pituitary gland is essential for life and the anterior or glandular position is most important.

Characteristic Features of Acromegaly.—*Acromegaly is a condition in which there is hyperpituitarism, which leads to marked increase in the size of the face, broadening and prominent jaw and overgrowth of the extremities*—the hands and feet particularly. If acromegaly develops before epiphyseal union *gigantism* results. When, as in the adult, the bones of the face and extremities are mainly involved the picture of acromegaly is presented.

Cushing's conception of acromegaly is expressed in the following paragraph:

"The disease, in short, is the expression of a functional instability of the pars anterior, doubtless brought about by some underlying biochemical disturbance which leads to the elaboration of a perverted or exaggerated secretion containing a hormone that accelerates skeletal growth (of the long bones if epiphyseal union is incomplete, of the acral parts if epiphyseal ossification has taken place)." . . . "A subsequent recrudescence with resumption of the perverted functional activity will then serve to superimpose acromegalic manifestations on primary gigantism." "Acromegaly cannot precede gigantism" but "always occurs as gigantism which has become acromegalized."

The disease is not frequent. In an active hospital and consulting experience of over thirty-five years I have seen less than ten cases.

Operative Treatment.—The question of the primary change which leads to acromegaly is of vital importance for prognosis; if it can be established that B. Fischer is correct that the complex is due to hyperfunction dependent upon adenoma and that no other growth causes hyperthyroidea, then operative treatment—the removal of the enlarged gland—

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offers the only hope of relief or cure. The disease is progressive and in the end fatal, though years of latency have prolonged the lives of the majority of cases seen in Central New York. Ocular symptoms—optic atrophy—are due to pressure of the growing adenoma.

Schloffer first suggested operative interference as a means of checking acromegaly and his case was relieved of its discomforts, and the acromegalic manifestations also showed marked improvement. Hochenegg has reported similar experiences.

Cushing's experience which is large should influence our conclusions in this country. His views are conservative, and he is opposed to operative interference in the absence of progressive symptoms ("degree of hyperplasia sufficient to cause neighborhood symptoms"). He believes that it is doubtful whether operative measures "can hold out any promise of permanently controlling the disorder." On the other hand, he believes that with "neighborhood symptoms" (pressure) due to "extreme enlargement of the gland due to the formation of an adenomatous struma whether or not there have been antecedent symptoms of acromegaly, the surgical aspects of the matter stand on a firmer basis."

Course of the Disease.—The rule may be accepted that with the gradual advance of the disease the facies in all acromegalies are similar, the bony growth is characteristic, the chin advances more and more, the teeth are widely separated, kyphosis is always prominent, the larynx enlarges, the nose broadens, lips are thick, tongue abnormally large, sexual function is likely to suffer—impotence is the rule in the male, in the female amenorrhea is frequent and there is involution of the uterus and its appendages.

The symptoms referable to the nervous system which show progression are increasing apathy, changed reflexes with increasing pressure symptoms, headache, vertigo, convulsions at times, optic atrophy, choked disk with increasing atrophy, amblyopia, bitemporal hemianopsia and cardiovascular changes, arteriosclerosis, dilatation of the ventricles and myocardial degeneration.

In the advanced cases there is enlargement of the liver and spleen. The blood shows eosinophilia and monolymphocytosis. There are *acute cases* which run a comparatively short course. *Sudden exacerbation of symptoms* is unfavorable and may lead to rapid growth and grave nervous manifestations—coma, meningeal symptoms, cerebral edema. Sudden heart weakness or death after several years of gradually increasing symptoms may follow acute infection.

Prognosis.— In the present state of our knowledge I am forced to offer a doleful prognosis for cure—medicine is of no avail; surgery offers only the hope of symptomatic relief during varying periods, though with our present experiences as a basis for surgical treatment the outlook for the future is reasonably encouraging. Animal experimentation and close

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clinical study with the laboratory as a helpmate are demanded to bring us to the scientific solution of this subject.

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C. Diseases of the Suprarenal Gland

Addison's Disease

See Tuberculosis of the Suprarenal Bodies

D. Diseases of the Thymus Gland

1. Hypertrophy
2. Atrophy
3. Status thymo-lymphaticus.

1. Hypertrophy

In the consideration of the diseases of the ductless glands I called attention to the frequent *enlargement of the thymus* with *goiter, exophthalmic goiter, acromegaly, suprarenal diseases, rachitis,* and with *myasthenia gravis* in which various observers have found infiltration of the gland and the skeletal muscles with lymphoid cells and marked productive change in the thymus tissue. I have seen sudden and fatal enlargement of the thymus with acute hyperthyroidea, also in one case of Ebstein's glandular

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fever. There are cases of *asthma of thymic origin* which have been relieved by surgical intervention.

In children sudden hyperplasia of the gland with or without other lesions may promptly cause death (*thymus death*). When the enlarged thymus compresses the trachea (*substernal struma*) asphyxia may cause death. *Sarcoma—lymphosarcoma*—may invade the thymus, also *carcinoma. Enlarged thymus with Hodgkin's disease* occasionally leads to prompt death.

Surgical intervention offers a fair prognosis in substernal struma and innocent thymus hyperplasia. The prognosis is absolutely bad in secondary enlargement which, when present, hastens the end.

2. Atrophy

Atrophy of the thymus is not of great clinical significance, so far as we know at the present time. It has been found with wasting of other organs, marasmus after gastro-intestinal drain and with syphilis (congenital). The clinician will not be called upon to offer prognosis based on atrophy of the thymus, for the condition is not diagnosticated *intra vitam.*

3. Status thymo-lymphaticus

Lymphatism

Kopp, in 1855, called attention to *sudden death* in *young subjects with cyanosis and stridor* in which the post mortem showed only the *enlarged and hyperplastic thymus.* In 1889, Paltauf called attention to sudden death in which there was, with *hypertrophy of the thymus gland, lymphatic enlargements throughout the body and abnormally small arteries.* In all of these cases death resulted in a few minutes.

The *"status lymphaticus"* has been established by Paltauf—a lymphatic diathesis which may lead to sudden death in children under a variety of conditions. Such children may die suddenly while under an anesthesic or from insignificant causes. There is a familial type of the status thymo-lymphaticus in which it is found that several children of a family die suddenly with like symptoms on slight cause. The status lymphaticus and enlarged thymus are intimately associated and the abnormal growth of the latter in a child ought always to be considered in connection with surgical or other risks. von Sury has found bronchiolitis ("capillary bronchitis") (?) a frequent accompaniment of thymus death. Sudden death during thyroidectomy is usually due to the status thymo-lymphaticus (See Exophthalmic Goiter).

There is a tendency to separate the status lymphaticus and the status thymo-lymphaticus; if differentiation is indicated, it is practically impossible because the status lymphaticus cannot be recognized by the

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clinician as a clinical entity ante mortem, and the enlarged thymus and status lymphaticus are almost always found together. In both death is sudden; in both there is lymphatism.

The *blood picture* which is characteristic of most deep changes of the ductless glands is found with the lymphatic diathesis—relative and absolute reduction of neutrophylic leukocytes and increase of mononuclear lymphocytes; in severe cases increase of preceding eosinophilia.

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E. Diseases of the Parathyroid Gland

Tetany

(*Tetanilla, Tetanie, Intermittent Tetanus, Status parathyreoprivus, Hypoparathyreosis*)

Definition.—Frankl-Hochwart's definition of the disease has been generally adopted by the profession. He considered its leading manifestations "tonic, intermittent, bilateral, often painful cramp, which without (as a rule) loss of consciousness, involve the muscles of the arms and hands particularly, which latter are held 'wedge shaped' or in the obstetrical position." The cramp is not always limited to the upper extremities but may include the legs, at times the jaw, the larynx, the face, rarely the thorax or other parts of the body (abdomen, neck, diaphragm or tongue). We now lean to the theory that tetany is often due to altered function of the parathyroid bodies.

Characteristic Features.—The bilateral symmetrical tonic spasm of the muscles associated with pain and paresthesias are the characteristic features, with the obstetrical hand, the Trousseau phenomenon (reproduction of the spasm by applying pressure to the arm above the elbow), the Chvostek phenomenon (producing muscular contractions of the facial muscles by tapping over the branches of the facial nerve) the Hoffman's symptom (abnormal hypersensitive sensory nerves as shown by the produc-

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tion of severe pain on tapping the Valleix's points) and Erb's phenomenon (hyperexcitability of the motor nerves to electrical stimulation).

Occurrence.—True tetany is an exceedingly rare disease in the United States. I have met but four cases in adults—three of which were secondary and due to gastro-intestinal lesions. Most cases seen in this country are of secondary and gastro-intestinal origin to which condition Kussmaul called attention in 1872.

Forms.—In considering the prognosis of tetany, the division of the separate forms in the adult by Frankl-Hochwart, the leading authority on the subject, may be safely followed:

(a) Idiopathic tetany
(b) Gastric-gastro-intestinal tetany
(c) Tetany associated with the acute infections
(d) Tetany of the poisons
(e) Tetany of maternity
(f) Tetany of parathyroid disturbance
(g) Tetany of various nervous diseases.

MacCallum and Voegtlin conclude that in all of these forms the essential factor of tetany is found in the relation of the parathyroid to the calcium metabolism of the body; their researches which bear on the rôle which the calcium salts exert in connection with tetany are of exceeding importance, for they tend to prove that the "salts have a moderating influence on the nerve cells" and that the "parathyroid secretion in some way controls the calcium exchange of the body."

(*a*) *Idiopathic Tetany*

Characteristic Features.—This is the so-called primary tetany of the Germans—the tetany found in otherwise healthy individuals—the workman's tetany and the epidemic tetany. The tetanic spasm is limited to shoemakers, tailors and handworkers. It is acute at times with remissions, and these are likely to make the disease chronic. With return to the usual work of the patient there is, after a time, recurrence of the characteristic symptoms of the disease. It is particularly frequent among shoemakers —in Vienna 60 per cent of all adult tetany is found among them. The disease among artisans afflicted selects the months from January to April by predilection. Among workmen, if this disease is primary it appears between the twentieth and thirtieth year; if later it is not likely to be primary. There are occasional acute forms of primary tetany which yield to rest and treatment.

Remissions.—Frankl-Hochwart found 32 of 37 cases of primary (occupation) tetany, chronic and subject to relapse. Curschmann reports the case of a tailoress whom he treated after twenty years of remission. Re-

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missions and exacerbations are materially and favorably influenced by change of occupation.

Frankl-Hochwart has recently given a less favorable prognosis than formerly in this form of tetany which seems to recur in epidemic form. In his further observation of the cases he found that many had died directly or indirectly as a result of tetany or the primary disease in from four to eleven years after the initial symptoms. The resistance of the patients was reduced and they yielded more readily to acute disease than do normal individuals. Of 264 cases originally observed 55 were traced ten years or more. Of these 11 died early; of the remaining 44 but 9 were in good health; 37 were examined personally; 7 had chronic tetany; 19 had tetanoid symptoms and 2.3 of all had persistent tatany phenomena.

(*b*) *Gastric and Gastro-Intestinal Tetany*

The mortality of tetany secondary to gastric or gastro-intestinal disturbance in which the underlying factors persist (dilatation, ulcer, etc.) is between 45 and 75 per cent. Naturally the underlying disease must remain the paramount factor in prognosis. I have found that in recurring and severe tetany in which there seemed to me to be a toxemia from dilated viscera, the daily lavage and emptying of the intestinal tract and the stomach prevented the threatening spasm.

Suddenly arising *cardiac asthenia* may prove fatal. This condition is always a serious complication and should be so regarded in the selection of therapy which, as a rule, needs to be radical—i. e., surgical.

(*c*) *Tetany Associated With The Acute Infections*

Among the acute infections which may occasionally be complicated with tetany are typhoid fever, cholera asiatica, measles, scarlet fever, tonsillitis, acute tracheal catarrh, laryngitis, polyarthritis and malaria, rarely influenza.

In the majority of these cases the infections are benign and the outcome favorable. In most cases there is but one seizure and the prognosis of the primary disease is not influenced thereby.

(*d*) *Tetany of Poisons*

The physiologic effect of poisons including chloroform, morphin, ergot, phosphorus, lead, urea and other renal and genital intoxicants may include tetanic symptoms. Tetany is mentioned in connection with novocain poisoning (Curschmann), cocain and atropin. Chvostek has seen tetany after tuberculin injection. Curschmann doubts Frankl-Hochwart's conclusion that tetany may be caused by alcoholism.

Prognosis.—The prognosis of this type of tetany must naturally depend

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upon the ability of the attendants to combat the acute poisoning promptly. In occasional cases *lead* may cause tetany. The prognosis of such cases is not materially influenced by the presence of tetany, unless the patient is already reduced or there are other grave effects of the poison.

(*e*) *Tetany of Maternity*

The tetany of maternity is more frequently met than was formerly supposed. This form of tetany is never to be lightly regarded. It is always a serious complication and is most frequent during the sixth to the eighth month of pregnancy. Once established the condition may persist until delivery; most women who recover are similarly afflicted during succeeding pregnancies. Occasionally a woman dies suddenly during an acute exacerbation.

(*f*) *Tetany of Parathyroid Disturbance*
(*Tetania strumipriva*)

The consideration of this form of tetany belongs to the surgeon. *Tetania strumipriva* is the gravest of all forms and may lead to death after thyroidectomy and the removal of the parathyroid bodies in a few days or weeks. Tetany may follow thyroidectomy within a few hours, or several days may lapse before the strumipriva is fully developed. If the entire parathyroid substance has been removed the prognosis is almost uniformly bad. von Eiselberg claims that partial thyroidectomy may occasionally cause tetany and reports 2 cases among 356 partial extirpations (See Exophthalmic Goiter).

(*g*) *Tetany of the Various Nervous Diseases*

Primary Disease.—Tetany occasionally accompanies *epilepsy, Basedow's disease* (*hyperthyroidism*) *myxedema* (*hypothyroidism*) *tumor of the brain, syringomyelia* and *cysticerci.*

The presence of tetany when limited to the hands and arms, without cardinal symptoms and without respiratory spasm, is not *per se* of grave moment; the prognosis should be based on the nature and extent of the primary disease. Attention should be called to the possibility of latent tetany with hypothyroidism. In such cases the Chvostek phenomenon is present. Such cases usually yield to treatment with the organic (thyroid) extract—the tetany disappearing as the myxedema is relieved.

Prognosis.—The prognosis of *tetany in suckling children* and *during early life* is, as a rule, favorable. The complication is likely to be acute and disappears after a limited period—usually several weeks, occasionally one or two months.

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Chronicity may follow but is exceedingly rare. When associated with grave nutritional faults the prognosis is correspondingly grave. *Spasm of the larynx* may prove threatening.

Infantile convulsions are separately considered.

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F. Diseases of the Spleen

The larger number of lesions of the spleen are of secondary origin, are associated with the infections, constitutional and toxic states, each of which demands separate consideration; to each I give due consideration with the separate diseases.

The great importance of the spleen as a *hemolytic organ* receives separate consideration in connection with the primary anemias, splenic anemia, Banti's disease and liver cirrhosis.

1. Secondary Splenomegaly

(*Enlarged Spleen*)

The acute enlargements of the spleen are practically constant with the infections: typhoid, malaria, sepsis, pyemia, pneumonia, recurring fever, kala-azar and a variety of other conditions including the acute congestions associated with the acute forms of disease of the blood-producing organs (See Infections).

The chronic enlargements of the spleen are rarely primary as, is abundantly demonstrated by the study of the essential anemias, syphilis, tuberculosis, chronic malaria, various liver changes, chronic portal obstruction, with the various types of cirrhotic liver. To all of these separate conditions the reader is referred.

In almost all diseases in which there is secondary splenomegaly, there are no subjective evidences of its presence; the diagnosis is only made after physical examination of the patient. The prognostic significance of the enlargement taken alone is not as a rule paramount. There are grave infections in which the spleen is but slightly enlarged, while in mild infections the enlargement may often be surprisingly great.

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Prognostic Factors.—(a) PASSIVE CONGESTION.—Passive congestion of the spleen and consecutive enlargement may be associated with *valvular diseases of the heart, emphysema, cirrhosis of the liver, leukemia with final proliferation* and *leukemic infiltrate.* Leukemic spleens may hasten death by their enormous growth and the pressure which results.

(b) ABSCESS.—Abscess of the spleen may be *encapsulated,* there may be *small multiple abscesses* or there may be *purulent breakdown* of the enlarged organ with *pyemic or septic infection.* These forms of splenic abscess are associated with the graver *pyemic conditions,* sometimes with *puerperal phlebitis* or *pyemia, erysipelas or infectious endocarditis.*

(c) PERFORATION.—Perforation through the capsule may lead to *fulminating septic peritonitis.* In all of these conditions the prognosis is grave in accordance with the seriousness and extent of the primary infection.

(d) PERISPLENIC ABSCESS.—Perisplenic abscesses may invade the spleen, cause disorganization and seriously complicate conditions. Most of these cases are due to the perforation of ulcers of the stomach or duodenum, traumatism at times, with or without *subphrenic abscess.* The prognosis is always grave.

(e) PERISPLENITIS OR CAPSULITIS.—This is secondary to syphilitic infection, leukemia, chronic malarial poisoning or polyseroritis (Pick's disease, multiple serositis, zuckergusskrankheit) in which the serous coverings of these organs—liver, peritoneum, pericardium—are involved, with enlarged spleen and fluid in the serous cavities. These patients may live for years but the fluid reforms and they finally die after repeated tappings of exhaustion or intercurrent infection (See Polyserositis).

(f) TUBERCULOUS SPLEEN and (g) AMYLOID SPLEEN have been separately considered. The former is comparatively rare when we consider the large number of tuberculous subjects. Amyloid spleen is a part of a general amyloid degeneration in which the blood vessels (arteries) are primarily involved after long-continued drain due to suppuration, tuberculosis, syphilis, bone disease or other infection. The kidney and vital organs are insufficient, and death is the rule in all such cases.

(g) SYPHILIS OF THE SPLEEN.—Syphilis of the spleen (See Syphilis) may cause enlargement. Gummata are not infrequent. Syphilis of the spleen is more frequent than is generally supposed and offers a favorable prognosis.

(h) UNCOMPLICATED ENLARGEMENT OF THE SPLEEN IN OTHERWISE HEALTHY SUBJECTS without subjective symptoms, accidentally discovered, will often remain unexplained. This condition is permanent and does not interfere with the general condition; neither does it cause discomfort or shorten life.

(i) CHRONIC ENLARGEMENT OF THE SPLEEN WITH POLYCYTHEMIA IS separately considered (See Polycythemia—Osler's Disease).

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(j) ENLARGEMENT WITH LIVER CIRRHOSIS.—The prognostic significance of *secondary enlargement of the spleen with alcoholic cirrhosis of the liver, syphilis of that organ* and *hypertrophic cirrhosis of Hanot,* is separately considered (See Diseases of the Liver).

(k) RUPTURE OF THE SPLEEN.—Rupture of an enlarged and infected spleen may occasionally happen with typhoid or malarial infection. In these cases the prognosis is bad.

The larger number of ruptured spleens follow *traumatism* and if promptly recognized and surgically treated offer an encouraging prognosis. Peritonitis and depletion are the leading dangers in neglected cases.

(l) CYST OF THE SPLEEN.—This is a surgical condition which, when innocent, offers a favorable outlook after radical treatment (See Echinococcus Disease). Operations for splenic cysts are almost uniformly successful.

(m) INFARCT.—*Enlargement of the spleen with hemorrhagic complications, multiple infarct,* more or less involvement of the sensorium, is always indicative of *malignant infection.* In all such cases *malignant endocarditis* should be suspected; *coagulation necrosis leads to disorganization and perisplenitis may complicate unfavorably. Recession of the enlarged spleen with acute or chronic conditions* may, in the majority of cases, be interpreted as being favorable.

2. Primary Splenomegaly

(*a*) *Splenomegaly of the Gaucher Type or Gaucher Disease*

(*Primary Endothelioma of the Spleen*)

Gaucher, in 1882, first called attention to splenomegaly of familial type in which the pathology has since been firmly established by the painstaking work of Stengel, Brill, Mandelbaum and Libmann, proving it to be *primary endothelioma.* Brill insisted that the Gaucher type of splenomegaly ought not to be considered in the category of splenic anemia because of its "unique and typical" pathology and "destructive clinical picture." In all cases of familial splenomegaly of the Gaucher type the splenomegaly is associated with corresponding increase in the size of the liver. Brill, Mandelbaum and Libman reach the following conclusions and I quote these because I have had no personal experience with the disease:

"Splenomegaly (Gaucher type) is a distinctive disease starting in early life, often affecting several members of a family and running a chronic course. It may be recognized by a great enlargement of the spleen, which precedes a similar enlargement of the liver, and is unaccompanied by jaundice or ascites; by the discoloration of the skin, especially where exposed to the light; and by the absence in the blood of any characteristic findings. The disease has none of the charac-

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teristics of malignancy and usually terminates as the result of an intercurrent infection. The organs affected are the spleen, liver, lymph nodes and bone marrow. Histologically these organs show the presence of large cells with small nuclei and a peculiar hyaline cytoplasm which arises from the endothelium or normal reticulum and the presence of pigment containing iron. The etiology is unknown, though a peculiar susceptibility of the endothelium or reticulum of the hemapoietic apparatus to some unknown toxic agent is most likely present."

There was nothing in the cases reported which suggested tuberculosis, "when found in cases of this disease, it must be considered as a superimposed process."

The chronicity of Gaucher's disease is striking. Naegele reports a case which had existed 39 years. Anemia is the fate of these splenomegalics with a strong tendency to leukopenia.

(*b*) *Banti's Disease—Splenic Anemia*

Characteristic Symptoms.—Banti's disease is characterized by enlarged spleen of unknown origin associated with splenic anemia, marked tendency to hemorrhages, esophageal varices, in most cases cirrhosis of the liver with jaundice and ascites in which the anemia is due to the hemolytic action of the spleen and in which the progress of the disease is readily controlled by early splenectomy. The splenomegaly is marked, the spleen is hard and smooth, painless and continues so throughout the disease.

Blood.—The blood count in the average case shows the characteristic features of *secondary anemia, marked hemoglobin* loss and striking *leukopenia.* In two of my cases the white count was as low as 800 and 1,500 per c. mm. respectively. My average red count has been between 2,500,000 and 3,000,000 per c. mm. After hemorrhages the erythrocytes reach low levels, while the leukocytic count is raised. One of my cases died of *esophageal hemorrhage.* At post mortem a *varix* was found eroded. *Repeated gastric and intestinal hemorrhages* influence the forecast unfavorably. The prognosis is bad in the cases which are far advanced and show *hemorrhagic tendencies with cutaneous and visceral purpura.* In *favorable cases* the splenomegaly persists during many years without liver cirrhosis (these are the cases of uncomplicated splenic anemia), moderate anemia with leukopenia and without hemorrhage.

Deep jaundice is rare; when present is an unfavorable symptom and is coincident with either marked degeneration of liver cells or the destruction of large numbers of red blood corpuscles. *Moderate jaundice* does not influence prognosis unfavorably and may persist with enlarged spleen and moderate splenic anemia during long periods. The growth of connective tissue in the liver may be exceedingly slow and is often without increase of subjective symptoms—during many years.

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Ascites is never to be interpreted as favorable. It usually proves the presence of *portal obstruction dependent on advanced liver cirrhosis.*

Albuminuria with casts or positive evidences of *nephritis, toxic symptoms (involvement of the sensorium), myocardial weakness or degeneration* are *all unfavorable.*

In the present state of our knowledge I would include all forms of splenomegaly of primary origin not due to new growths (carcinoma, sarcoma or the Gaucher endothelioma) in the class of *splenic anemias* of which Banti's disease with advance to liver cirrhosis represents the full development; in other words, *splenic anemia is a chronic primary splenomegaly of the infant (von Jaksch anemia splenica infantum) or adult, associated with marked anemia and striking leukopenia.*

Prognosis.—All splenic anemias are persistently chronic and all offer a good prognois when the hemolytic organ—the spleen—is removed, without its removal the prognosis for cure is bad—not always fatal. It is of the utmost importance for the clinician to appreciate the fact that the cirrhosis of the liver with splenomegaly or splenic anemia is of secondary origin, dependent in some way upon the primary disease of the spleen.

Splenic anemia in children may prove to be self-limited and may lead to full recovery with recession of the spleen. The author has seen several such cases and medical literature offers abundant examples (See References). The degree of the anemia should not always be taken as the guide for prognosis.

3. Mobile Spleen

Movable or mobile spleen may give rise to no symptoms and is often accidentally discovered. It is more frequent in women than in men and is usually a part of Glenard's process with enteroptosis, gastroptosis and gastrectasia—often mobile liver as well. Mobile spleen may cause discomfort but never seriously interferes with the normal processes of the individual. Mechanical devices and, in extreme cases, surgical interference will bring relief.

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Section XI

Intoxications

1. Alcoholism

(a) General Consideration of the Alcohol Habit
Excessive Use of Alcohol
Intoxication Impulse (Lambert)
(b) Acute Alcohol Poisoning
(c) Chronic Alcoholism
(d) Delirium Tremens.

(*a*) *Alcohol Habit*

Intoxication Impulse

(Lambert)

General Considerations.—In the preparation of this chapter the author has been materially assisted by Alexander Lambert, of New York, who, in the management of his large material at Bellevue Hospital, has demonstrated his superior knowledge of the subject, his tact and humanity. The author wishes to thank Doctor Lambert for his assistance which he gladly acknowledges, and feels at liberty to base his conclusions as they affect prognosis upon data liberally supplied by Doctor Lambert and the result of his own hospital and private experiences.

We assume that the alcohol habitué has, as the result of his habit, disturbed "the equilibrium of health," that his tissues are so changed as to justify the conclusion that he is out of health; in other words, after the excessive and continued use of alcohol as it is taken by the chronic drinker, a changed condition of the central nervous system—more particularly the brain—develops which *robs the victim of will power sufficient to resist the impulse which leads him to drink. Without the assistance which the physician extends to every human being whose will power is paralyzed or who is suffering from a disease which makes it impossible for him to help himself unaided, and without sufficient remnant of will power to*

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make the victim will and divorce himself from the slavery which holds him, there can be no hope of emancipation.

No victim of the alcoholic habit can be cured permanently who is so blunted, so diseased that he remains absolutely passive, without the desire to be cured. The *perverted mind—changed psychic function*—must be brought under control before lasting benefit from any form of treatment can be expected. The brain cells are altered by the long-continued or even periodic use of the poison—as Lambert says: "If we fail to unpoison the individual, we will surely fail in our cure of him."

Personality and will are both poisoned; the mind thus poisoned cannot act normally; it is without will power and must remain so until *unpoisoned*—when the foundation for release has been established.

The use of alcohol in small doses by the worker in any field of activity will ultimately lead to larger doses (in most cases) and the development of the alcohol habit. Chronic alcoholism often follows the repeated convivial drinking in those "who drink to increase the joys of life." Lambert does not believe that this tends to chronic alcoholism so often as do other forms of drinking, but we are agreed that it does finally lead to steady drinking which becomes excessive and in many, chronic alcoholism follows. There is a third and large class which we meet in hospital and private practice in which because of inherent weakness—bad heredity—the slightest disappointment or extra tax, physical or mental, leads to the use of alcohol. The added reserve which may follow the initial small dose encourages repeated drinking until the habit is fastened, the mental processes grow more and more satisfactory to the deluded victim, while in truth, judgment, memory, expression and physical force are all influenced unfavorably and in the end, the subject is so enslaved that he does nothing without alcohol and becomes a chronic alcoholic.

This is the history of the development of the alcohol habit in doctors and lawyers. The former, wearied by long vigil, drinks to gain "artificial stimulation" that he may finish the day's work; the latter in the trial of a case, seeks the "brace" which he believes will carry him through. In all of these, *the psychic element becomes the paramount issue.* "Judgment, reasoning, memory" and will power one after the other depart and there is left "an emotional creature" no longer dominated by normal psychic processes—sound reasoning—but swayed by sentiment with increasing mental decay, without initiative, who falls and feeds his diseased nervous system with the poison which his perverted appetite craves.

Alcoholics, like all who are enslaved by other narcotics, are ready to subject themselves to the influence of any drug which will bring that exhilaration or paralysis so much enjoyed when the brain has become thoroughly poisoned. Mental breakdown with alcohol and morphin or with both and cocain is prompt, the entire personality is changed and

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the moral sense blunted. Hope of release is offered by eliminating from the memory of the habitué the continuous physiologic and pathologic effect which creates the appetite for the drug. This can only be accomplished by thorough divorce from the poison. The physical and mental restoration are often slow—for there is in all that psychic state which is persistent, full of torture, with a panoramic view of the hours of dream which invite recourse to alcohol, against which a strong will is needed. Once released or "unpoisoned" much depends upon the physical status of the patient, the environment, the social condition and above all, upon the assistance which the habitué gives himself.

Influencing Factors.—*Heredity* is an important factor; it influences the resistance, the amount of mental vigor and the personality of the individual and affects the basis on which the addiction is built. I am fully agreed with Lambert that a weak personality poisoned by any drug will be a difficult subject to release. The prognosis is unquestionably influenced unfavorably by alcoholic inheritance. "It would seem that we should find an expression in the individuals of today in their actions toward alcohol and their reaction to the impulses leading to intoxication which shows the development and racial use of alcohol in the past." The *"intoxication impulse"* is "an expression of the social instincts of the individual," "an expression of vigorous youth straining to enjoy the teeming abundance of sensations" (Lambert). Uncontrolled, this impulse, inherent in the race, "drives the individual on and overpowers often the instincts of self-preservation and self-interest."

In *early vigorous manhood* (early twenties) excessive drinking in those not burdened with an unfavorable heredity or provoking factors, as seen "in college students and in youths of that age" is not as a rule an expression of paralyzed will, and in the end, before there is addiction, the majority escape. The prognosis depends largely on the *personality* and many factors in these subjects. *Early training—discipline*—proves of enormous prognostic influence. The man, who in middle life drinks deliberately that he may become intoxicated, who seeks periods of effacement, is among the most hopeless of all drinkers. He seeks the narcotic and soon he longs for its continuous effect.

Periodic drinkers are among the most unfortunate of drinkers. In them, the intoxication impulse is sustained by the memory of past debauches and an eager desire to escape from their surroundings. Their psychic anomalies are often remedied with the greatest difficulty. The will seems to be paralyzed in cycles and there is an instability which is easily recognized, the features of which it is difficult to explain. Many periodic drinkers are physically sick; they are often poisoned by toxins which they elaborate or which they add. Lambert believes that "the majority of periodic drinkers who are endeavoring hopelessly to cease their periodic sprees are really cases of chronic tobacco poisoning." Cigarettes

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more frequently than the pipe or cigars are the cause. "Double narcotic poisoning" is often cured by release from the primary poison which leads to the final intoxication.

Psychoses are often responsible for periodic drunkenness. The manic-depressive condition, which is recurrent, invites that indulgence which divorces the diseased mind from a state of depression and one of less gloom to practical oblivion. The prognosis of such conditions naturally depends upon the ability to control the mental element (alienation).

Lambert reports 1,019 patients treated for alcoholism (habit) with 105 relapses—10 per cent. Some of these relapsed once or twice and are now permanently released, having returned to their occupations "sober members of the community." He reports 80 per cent successes in his final analysis—20 per cent failures. In my own experience, I have, because of a different clientele, been less successful. Many of my cases have come from country districts and not a few have been addicted to the use of morphin, cocain, one or both with alcohol. I have found the *element of time* of great importance in prognosis. Those cases which have left the hospital or observation before restoration of physical strength or the relief of diseased conditions or who have returned to be subjected to annoying and complicating problems have lapsed early and have continued unrelieved.

Excessive Use of Alcohol as Exciting Factor in Many Diseases.—The prognosis of many diseases is materially influenced by the excessive use of alcoholic drinks. This is particularly true of tuberculosis and syphilis (See Section I—Tuberculosis and Syphilis). There are suddenly arising complications in which alcohol finally proves to be the exciting factor, in which the habit had never been suspected.

Tolerance.—*The daily quantity of alcohol* which may be taken without bad effect varies with different individuals; this variation is influenced by the general condition of the subject and varies at different times under changed conditions in the same individual. *Sedentary occupations* reduce the tolerance for alcohol and invite consecutive chronic changes. In my consideration of acute and chronic alcohol poisoning mention is made of the organic changes which influence the clinical history.

Conclusions.—In my practice I have learned to place the greatest reliance on the results of a thorough investigation of the life history of patients, a study of their antecedents, their environment, a full understanding of their social and daily problems. In hospital practice this is, as a rule, impossible, but it becomes the function of the social worker to lead in this crusade which promises to save a large number of these unfortunates. In private practice the prognosis of the alcohol habit is better in proportion to the ability to supervise the life of the patient. The strong personality of the physician will always prove a powerful factor in leading the victim. The diseased mind and body demand surveillance and treat-

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ment; each case becomes a psychic study; each life demands that rearrangement which will lead to mental and physical health in an environment which will be most likely to reduce depressing factors during long periods. This is a monumental task but with proper organization it promises sufficient success to justify the trial.

(*b*) *Acute Alcohol Poisoning*

Ordinary *acute intoxication* following the use of alcohol as seen in the average case of drunkenness after a period of cerebral paralysis (stupor) following psychic excitation, increased frequency of the pulse (as a rule), involuntary discharge of urine and feces, disturbed respiration, dilatation of the pupil, cyanosis, clearing of the sensorium, leaving the victim with tremor, headache, nausea, muscular weakness, gastro-intestinal disturbance during periods varying from a few hours to several days—all depending largely upon the size of the dose, idiosyncrasy, age, the duration of the habit and the extent of secondary changes which follow long periods of preceding inebriety with repeated acute exacerbations (poisoning).

Associated Conditions.—The leading dangers are due to *exposure, accident, infection, cardiovascular disease* and *complications* referable to the *central nervous system, liver* and *kidneys.* In hospital practice drunkards are often brought in with frozen extremities, final deep sloughs, and in bad cases loss of fingers, toes and occasionally one or more extremities. In these cases convalescence is slow and exposure is not infrequently followed by *alcoholic pneumonia* associated with *meningismus,* often with *delirium tremens.* As a rule with alcoholic pneumonia there is extensive infiltration; *the prognosis of pneumonia with acute alcohol poisoning is bad*—over 80 per cent die.

Alcoholic Poisoning.—There are but few deaths following acute alcoholic intoxication in which the lungs are found without evidences of inflammation—infection. Many are brought into hospitals with acute delirium and with injuries sustained while intoxicated. In these, there is danger of infection; erysipelas, sloughing, gangrene and reparative processes are tardy. In one case, which had been acutely poisoned during several days a hernia became strangulated, remained unrecognized and led to death. Acute alcoholic poisoning may lead to *sudden death* in the subjects of *chronic cardiovascular* disease, often with fibroid or fatty hearts, or with degenerated hearts in chronic nephritics. In one of my hospital cases a young woman who had been acutely poisoned, who was not addicted to the use of alcohol, I found after a few days of wet brain fully developed multiple neuritis with quadriplegic paralysis and before the end of the seventh day she died of acute atrophy of the liver.

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Changes Due to Poisoning.—The development of *acute nephritis* or *acute exacerbations of chronic nephritis* following alcohol poisoning may seriously menace life. In those suffering from chronic disease of the nervous system, acute poisoning produces profound changes, often threatening. Epileptics are promptly affected and unfavorably; idiots develop alarming meningeal and peripheral symptoms; acute poisoning in the injured is always of serious significance, while the prognosis in those convalescent from the infections or from surgical operations is always grave. Small doses of alcohol are often sufficient in these to promptly provoke symptoms; in health large doses would be required to cause the same results.

The drinking at once of a large quantity of alcohol may promptly cause collapse and death. In some cases death may not follow; in such cases for several hours during which the local effect of alcohol on the gastric mucosa leads to vomiting, retching and increasing heart weakness results.

In cases in which either with suicidal intent, by accident or to produce a prompt drunk, the victim swallows a large quantity of alcohol, the prognosis will depend very largely upon the *promptness with which the stomach is emptied and absorption prevented.*

Cerebral apoplexy and *thrombosis* may develop during acute alcohol poisoning, as may *uremia* in cases of chronic nephritis. I have seen death from *coronary spasm, thrombosis of the coronaries,* and unrecognized *dilatation of the stomach* during acute alcohol poisoning.

Symptoms referable to the nervous system (neuritis and meningitis), the gastro-intestinal tract, the genito-urinary and cardiovascular organs, may persist during long periods after acute poisoning; these in the previously healthy usually yield (See Alcoholic Neuritis—Section VII).

(c) *Chronic Alcoholism*

Psychic Element as Leading Factor.—In the general consideration of this subject I insisted that the alcoholic habit is nurtured and sustained by an abnormal psychic state. Whatever the conditions which lead to the formation of the habit—and it is more likely to develop in those with lowered resistance, inherent weakness (hereditary influences)—ultimately the psychic element in all stands prominently in the foreground and as already suggested (general considerations) the prognosis depends upon the recognition of this fact.

Productive and Degenerative Changes.—The chronic alcoholic is persistently below par. He is without normal resistance to disease, is more subject to all diseases—constitutional, local and infectious—than is the normal individual, and when the habit has existed during a considerable period there are productive and degenerative changes which increase insidiously, often unnoticed during long periods, because of the absence of

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subjective symptoms, which are often so deep and far-reaching as to make restitution impossible. The leading changes produced by chronic alcoholism are referable to

(a) The gastro-intestinal tract
(b) The nervous system
(c) The liver
(d) The circulatory system
(e) The genito-urinary system
(f) The organs of special sense
(g) The respiratory system.

(a) Gastro-intestinal Tract.—But few chronic drinkers are without change in the gastric mucosa. This may be productive, atrophic; and, when the habit has not continued long, subacute gastritis with or without proliferative change may be present. The *intestinal changes* are less marked, but in advanced cases, atrophy of the follicles and irregularly distributed hyperplasia are not uncommon. The prognosis of alcoholic *gastritis* and *enteritis* is good in cases which can be controlled. It is surprising to find how promptly the "morning vomiting" of the chronic drunkard yields (See Gastritis—acute and chronic).

In chronic cases *polypoid growth and pyloric hyperplasia* (stricture) may lead to continuous symptoms which refuse to yield, and for surgical interference offer an unfavorable outlook. *In all forms of surgical complications the prognosis is unfavorable, compared with the non-alcoholic subject.*

The *chronic pharyngitis* of the drunkard does not yield to local treatment, it does yield to discontinuance of the poison. *Duodenal and gastric ulcers* may develop during active gastro-intestinal symptoms or may have existed before the alcoholic gastritis. I have no case of perforation to report. The prognosis of the stomach lesion *per se* has been the same as without alcoholism. None of my cases were operated.

(b) Nervous System.—The complications referable to the nervous system have been separately considered in the various chapters of Section VII, dealing with *alcoholic multiple neuritis, amblyopia, optic neuritis* as well as *other changes in the cranial nerves, the meningitides,* also *wet brain and encephalitis;* to these the reader is referred. The general statement may be made, that in favorable surroundings with corrected habits the prognosis of these conditions is often surprisingly good. This however is only a general conclusion and in each of the conditions mentioned demands such modification as is fully considered in the separate chapters to which I refer.

The *psychic disturbances* depend for their prognosis upon the extent of the organic change which the long-continued use of alcohol has caused (See Encephalitis, Wet Brain, Epilepsy, Neurasthenia, Hysteria, etc.).

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In hospital practice long-continued psychoses may finally yield permanently; in some there is a remnant of symptoms which remains.

Korsakoff's psychosis may complicate delirium tremens or chronic alcoholism without marked mania. Patients with the complex are usually delirious, have multiple neuritis and the characteristic memory defect. There is inability to orient, failure to retain new facts or impressions, loss almost entire of the recent past and in some cases retention of only isolated events of the remote past. The loss of memory of the day's events is prompt and early demonstrated in a test of but a few minutes. The psychosis is usually chronic, the polyneuritis is likely to mend before the memory improves. In subjects who recover it is often noticeable that they retain their habitual social forms, while their real personality is burnt out; you seek for it in vain. It is a curious condition. Talking to them superficially, to be with them in superficial things, they appear perfectly normal, but try to reach the mainsprings of their personality and you find that it has been destroyed. Years may elapse before there is full return of memory—in some cases the normal may never be reached. The attending conditions (heart, arteries, kidneys, etc.) are paramount in the prognosis of the Korsakoff syndrome.

Oppenheim found 30 per cent of all alcoholics admitted to the Charité (the ward in which the delirious were confined) suffering from *epilepsy* (See Delirium Tremens).

(c) The Liver.—The lesions referable to the liver and their prognostic import are fully considered in connection with the various types of cirrhosis. Advanced cirrhosis is usually complicated with organic changes in other vital organs (stomach, kidney, heart and arteries) and materially influences the prognosis (See Liver Cirrhosis).

(d) Circulatory System.—The influence of alcohol on the *heart* and *arteries* has also been separately considered. Whether these changes are produced directly or indirectly their results are the same and prognosis is unfavorably influenced by their presence. Much can be done to influence these cases favorably in the presence of far-reaching changes in the circulatory organs mentioned. The coöperation of the patient with rational living is the important factor.

Degenerative heart changes (myocarditis—coronary sclerosis) with chronic alcoholism seriously complicate the forecast (See Diseases of the Heart, Arteries, etc.). The complication of *syphilis* with alcoholic change in the cardiovascular system and alcoholism is often provocative of lesions which involve the nervous system (paresis, tabes, etc.).

(e) Genito-urinary System.—*Changes of organic nature involving the genito-urinary system* often add a large element of danger. This is particularly true of cases with *enlarged prostate and urinary retention in which cystitis results from neglect,* in cases of *ascending infection,* with *calculosis*—either bladder or kidney—and with all forms of nephritis,

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particularly the chronic interstitial, in which there are at the same time advanced heart and arterial changes or in those forms of secondary contracted kidney with chronic uremia or recurring poisoning (See separate chapters—the Nephritides—Nephropathies).

(f) Organs of Specific Sense.—Organic or functional changes in the organs of special sense may cause prominent symptoms. *Ocular disturbances* are most frequent. The functional disturbances yield to rational treatment. *Optic neuritis, partial optic atrophy, central scotoma* for colors (red and green) and *loss of pupillary light reflex* in advanced cases may remain unchanged, though improvement may follow with the disappearance of separate symptoms in the less chronic cases under favorable conditions.

(g) The Respiratory System.—I have elsewhere referred to the bad prognosis of all pneumonias in alcoholics (See Pneumonia) and to the fact that pneumonic infiltrate is found in most alcoholics who die with either acute or chronic symptoms. The tuberculization of the alcoholic is comparatively easy. Many finally yield to this infection (See Tuberculosis).

In alcoholics *disseminated bronchitis, grippal infection, acute catarrhal invasion* of any part of the respiratory tract are easily complicated by broncho-pneumonia—always serious. The chronic bronchitis of the alcoholic is persistent and never yields until he has reformed during a sufficiently long period. In some, it persists in spite of the discontinuance of liquor; the same is true of alcoholic laryngitis and tracheitis.

(*d*) *Delirium tremens*

(*Mania a potu*)

Symptoms.—Habitual drinkers are subject to a complex of symptoms known as delirium tremens. This includes active delirium associated with muttering, continuous incoherent talking with hallucinations—almost always visual and aural—increasing terror as the condition develops, troublesome insomnia—often controlled with great difficulty—persistent tremor of all muscles and tongue increased by movement, rapid pulse (100-130 per minute) often dicrotic, usually febrile movement (101°-104° F.) and albuminuria in over 60 per cent of all cases.

Recurrence.—Delirium tremens once developed is likely to recur if the habit is continued. In my hospital service I have alcoholics who for years have returned to the wards as often as once in two months, usually leaving the hospital restored physically but with their psychic being unchanged.

Prognosis.—The prognosis of uncomplicated delirium tremens is relatively good. A mortality of 15 per cent represents the average of hos-

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pital practice. Statistics vary from 2 to 15 per cent (Oppenheim). In 709 cases of delirium tremens in Bellevue Hospital there were 143 deaths or about 20 per cent (Lambert); 61 of these died of pneumonia. There were 125 cases of pneumonia in the 709 cases. Deducting the pneumonias there were 584 remaining, with a death rate of 14 per cent. It is useless to compare the mortality of hospital with private practice. The former include the worst possible timber, the latter, well-housed, early escape the exposure and infection which kills. Moderate drinkers who develop delirium tremens easily, offer an unfavorable prognosis.

Persistently high temperature with delirium is unfavorable; if the pulse continues rapid and small with evidences of dilated heart and cyanosis, particularly in the plethoric, the prognosis is bad. *Obesity* is unfavorable in such cases. *Wild delirium with rapid pulse, dry tongue, albuminuria with casts and uncontrolled insomnia* is an unfavorable combination. *Involuntary discharge of urine and feces* is not necessarily significant though it attends the more serious cases.

Collapse at any time usually leads to death because of its primary cause (dilated heart, myocardial degeneration). *Infections of any kind are serious,* the more alarming as already mentioned, are *pneumonia, erysipelas, meningitis* and *suppurative otitis.*

Patients with "wet brain" who live beyond the second week, in my service as a rule make slow, but good, recoveries. With retraction of head and stiff neck, the prognosis is not good (Dana). We have only rarely committed a patient to a state institution from our wards, who on admission failed to show some evidences of preceding mental alienation.

Mild delirium persisting during several weeks does not affect prognosis unfavorably if without complications.

Duration.—The *length of the average delirium* is about 4 days; no time limit can be given.

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2. Morphinism

What has been written in this section of the underlying psychic anomaly in alcoholism is equally true of the morphin habit and it is also true that no morphinist can be saved from the bondage which holds him who does not earnestly assist in his own emancipation. Unquestionably recently enacted federal and state laws will prove powerful factors, if rigorously enforced, in reducing the number of drug habits; the medical profession has a large responsibility to shoulder in this connection. When we consider that one-third, at least, of all morphinists are physicians, we find ourselves face to face with a problem which should enlist our most careful study.

Prognosis.—Prognosis in the majority of those treated early, before the nervous system has been functionally ungeared, is good; it is discouragingly bad in the majority of chronic cases, particularly in those associated with central nervous disease, with sensory symptoms (tabes dorsalis, chronic neuritis) and with gastro-intestinal or any other disease in which pain started the use of the drug, including cholecystitis and renal calculosis. The prognosis of the morphin habit is always improved by the radical removal of the factor which causes pain, unless the habit has been long formed; it is always worse when morphin is taken without sensory symptoms demanding relief.

Course of Intoxication.—Like alcohol, the early small dose is gradually increased. In rare cases the initial dose is not increased during considerable periods and the general appearance of the patient and his health are not noticeably changed; sooner or later all morphinists increase the dosage and show the earmarks, promptly recognized by the experienced eye, which brands them as slaves to the drug. The physiological effect of the drug is sought; the color remains persistently sallow, the eye dull and pupils contracted; marked restlessness continues unless the fading effect of the preceding dose is met by a fresh injection or dose; the mental vigor for a time is increased, as the dose is increased and narcosis, more or less continuous, begins to fail; the moral sense is blunted, truth is no longer respected; the being is metamorphosed and often physically and mentally unrecognizable. Unkempt and neglected they live, often many years, always deceiving, untruthful, absolutely undependable.

I met one country physician in consultation who took a level teaspoonful of morphin sulphate in a single dose. He lived to be almost eighty years of age.

Influencing Factors.—The *size of the dose and the quantity* taken during twenty-four hours varies with the duration of the habit and with the individual. Lambert does not believe that the size of the dose has any settled ratio to the duration of the habit. The *sudden withdrawal of all morphin* from the chronic habitué may lead to *collapse*—alarming,

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even fatal. I have seen gastric symptoms and diarrhea during treatment and the withdrawal of morphin prove threatening and controlled with great difficulty. Most of my cases of morphinism have fallen into wretched states, have developed intercurrent disease—often infection.

The majority of habitués are handicapped by an *unstable nervous system* or *bad heredity*. This fact makes prognosis graver. *Psychopathic states* invite the habit and make the release exceedingly difficult.

The development of the habit among medical students is encouraged by a desire to learn the physiological effect of the drug; *this practice should be vigorously discouraged.* Successful issue demands months of surveillance and control, without which the prognosis for lasting cure is bad and relapse is the rule.

Meyer (E.) places the percentage of permanent cure at only 1 to 2 per cent. Levinstein reports 82 patients (males); of these 61 relapsed; of 28 women, 10 relapsed; of 32 physicians only 6 were released, 26 relapsed. The prognosis among physicians is discouraging. Hirt reports 27 of 35 morphinists cured. This is an unusually favorable outcome and has not often been equalled by the treatment of an equal number of average cases in America. *Suicidal mania* develops in a comparatively large number of cases.

I have been more successful in my cases, probably because many have been placed in hospitals, taken from depressing environments and remained under strict surveillance; then too, the cases which I have seen in private practice have been treated early. The material which we have in our wards is not favorable for ultimate cure; this includes many who are alcoholics, tobacco and cocain fiends, and among the women, a large proportion of prostitutes. They are without the remnant of moral force which is so necessary for success.

Accompanying Conditions. — *Arteriosclerosis, chronic constipation,* other *gastro-intestinal symptoms, myocardial insufficiency, sexual anomalies* (*perversion*), *irregular types of fever, final emaciation* (*marasmus*) with *terminal infections—septic, pyemic, tuberculous* and *pneumonic*—complicate chronic morphinism.

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3. Cocainism

Cocainism which has not persisted during a long time is more successfully treated than morphinism; if the drug has been used long, complete or lasting cure is unusual. Cocainism and morphinism are twin sisters —they frequently rule together, and alcoholism completes a trio of habits from which escape is exceedingly rare and difficult.

Cocainism which has continued during months drags the victim to the lowest level of morality; the change is so complete as to leave but little of his original brain power or personality. Hallucinations, paranoic symptoms and insane jealousies develop which with marked emaciation, occasional jaundice, persisting insomnia, pigmentation, optic disturbances, cardiac anomalies (tachycardia), irregular respiration, spasm of the neck muscles (oftener in acute cases), anomalies of the sweat glands and utter disregard for order, discipline, cleanliness, truth or tact often continue during months or years, the victim awaiting intercurrent disease, infection, accident or suicide to end his days.

I have seen a number of advanced cases of cocainism permanently cured. The struggle in such cases is fierce and the forces which invite relapse are powerful and usually conquer.

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4. Lead Poisoning

Acute Poisoning

The acute poisoning due to lead, usually the acetate and oxid, is infrequent, leads to gastro-intestinal symptoms of an irritating character, rarely to subacute or chronic symptoms and in almost all cases offers a good prognosis when rationally treated.

Chronic Plumbism

Chronic plumbism includes—

(a) Constitutional symptoms with lead colic
(b) Saturnine arthralgia
(c) Lead palsy

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(d) Lead encephalopathy
(e) Saturnine anemia
(f) Saturnine arteriosclerosis
(g) Saturnine nephropathy (Chronic interstitial nephritis).

Influencing Factors.—The influence of *heredity* on the development of lead poisoning has not been satisfactorily settled. It may be assumed however, that in cases where several members of a family or succeeding generations have been poisoned that all were exposed to corresponding conditions. We have positive evidences at our command which prove that *children are less easily poisoned than are adults* (shown by poisoned drinking water, cider, etc.) but when once surcharged they yield with greater difficulty—often resist cure during long periods more obstinately than do adults. In children *diarrhea,* a frequent symptom early, has a favorable effect.

Oliver proved that *women were more susceptible than men* and it has been noticed that their suffering is more acute. *Improper feeding, filth, carelessness* in the care of hands, teeth and utensils, *alcoholism, nephritis, sexual excess* and *faulty ventilation* are all inviting factors and increase symptoms.

(a) Constitutional Symptoms with Lead Colic

Occupational Influence.—Painters, carriage rubbers, lead workers, plumbers, potters (china workers), tea tasters, typesetters, polishers and glaziers are among the most frequent occupations which cause lead poisoning.

Constitutional Symptoms.—In all lead poisoning, whatever the symptoms, there are constitutional anomalies which are characteristic with changes in the blood of a degenerative character demanding consideration in offering prognosis. In my treatment of the subject I refer to the leading clinical pictures upon which prognosis may be safely based. The constitutional symptoms in cases with lead colic are less developed than with some of the other clinical types. This is so because in most cases of lead colic the poisoning has not become chronic and colic is one of the early manifestations.

Colic is due to spasmodic contraction of the intestinal musculature. While most cases show moderate *saturnine anemia,* it is not profound; as a rule, the cardiovascular changes in early cases are not developed, the *blue line* is likely to be present, the pulse shows some abnormal slowness, is tense, and lethargy is more or less marked. The colic itself is often severe and is associated with obstipation. There is vomiting, and the pain of the tense abdomen is often relieved by pressure and opium and in almost all uncomplicated cases, is cured when recognized and the source of poisoning is removed. Where the water supply is "lead charged"

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and the source is unrecognized, colic will return and other symptoms of plumbism develop. I have never seen death result directly from uncomplicated lead colic; cure has been the rule.

(b) Saturnine Arthralgia

Severe and persisting pains in the joints and neighboring muscles may complicate any of the clinical types of lead poisoning. It may however, be the only subjective complaint in occasional cases; it is usually associated with *anemia, tense and slow pulse,* often *elevated blood pressure* and occasional *albuminuria.* The knee is the favorite seat of arthralgia. The outcome of most saturnine arthralgias included in this type, associated with some of the less threatening organic changes of chronic plumbism, is good. It requires only the recognition of the cause and source of the pains and poison and common sense treatment.

More than one-half of the cases of lead poisoning which enter the hospital for treatment show evidences of lead paralysis and the majority of these have double *wrist drop.*

(c) Lead Palsy

I have separately considered the peripheral paralysis and neuritis due to lead (See Section VII).

The prognosis of most cases is good though in chronic cases remnants of paralysis may remain.

(d) Lead Encephalopathy

The cerebral disturbances dependent upon lead poisoning are included in the *lead encephalopathies.* There are cases in which the sensorium is never disturbed; others in which lead causes early brain symptoms, sometimes mild, in some severe and threatening. In some with colic or other positive organic changes moderate psychic disturbances are transitory, while in others—and these are *graver types—after long periods of plumbism there are psychoses or delirium, coma and death.*

In the majority of fatal cases the encephalopathies have been found in chronic conditions with cardiovascular and renal changes and usually with profound anemia. Subacute poisoning with *anemia gravis* and marked morphologic change of cellular elements of the blood, leukocytosis and abundant basophilic bodies have been most intractable and I have lost a number of these patients within the first two or three months following recognition and treatment. Long-continued plumbism with arterial change in subjects who continue at their work is often sudden, followed by encephalopathies, active mania, wild delirium and with evidences of failing heart, preceded by hypertension, these patients die.

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Encephalopathies (psychoses) which persist during long periods, unless they show some improvement following institutional treatment early, may never fully recover though there may be sufficient change to justify discharge from state surveillance. In all encephalopathies the associated conditions and lesions must influence prognosis powerfully. The delirium of profound saturnine anemia and the muttering or occasional delusions with lead colic and constitutional symptoms usually yield as the general status is improved.

Recurrence.—Encephalopathies are likely to recur with fresh poisoning and in such cases are obdurate, persist long after the more acute symptoms yield. There may never be a return to the normal standard.

Associated Conditions.—*Convulsions of an epileptic nature* are not infrequent and recur especially in the more chronic cases. In subacute and chronic cases *tremor* is often a prominent and occasionally remains a permanent symptom. I have seen a number of cases without encephalopathy in which tremor was associated with colic, hypertension or peripheral neuritis and palsy, in which with full recovery the tremor disappeared entirely. *Ocular symptoms* may develop with or without encephalopathies, including *optic neuritis, optic atrophy, neuro-retinitis,* and with advanced arterial change *choroidal hemorrhage.* In these cases the prognosis should be guardedly given, the case should be observed by the ophthalmologist. These complications are likely to accompany the more chronic types with cardiovascular and renal changes. Serious eye lesions are not frequent. De Schweinitz found only three in 15,000 eye cases. The addition of an *emotional element—hysteria* and *neurasthenia*—does not materially complicate the outcome, so far as life is concerned.

(e) Saturnine Anemia

Moderate saturnine anemia, as already stated, complicates most chronic lead poisonings. The milder anemias promptly improve under treatment and do not lead to persisting blood changes. The *graver anemias* are found in the more serious cases with mental torpor, often delirium, hallucinations and encephalopathies. These graver anemias are among the more serious complications of lead poisoning.

The Blood Picture of Lead Poisoning

Stengel, White and Pepper 3d, have after painstaking study of the blood concluded that there is no other poison which so regularly and promptly causes degeneration as does lead.

Naegeli believes that the pallor of the poisoned is due largely to vascular spasm and bases that opinion upon the frequent absence of chlorosis and low red count. My cases have usually shown moderate oligemia

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during the early stages, and increasing anemia as the condition became more chronic.

In chronic lead poisoning the average red count in severe cases will be found below 2,000,000—mild poisoning 3,000,000 to 4,000,000 with leukocytes between 10,000 and 20,000. Many normoblasts indicate severe anemia—.5 to 3.4 per cent (Becker, Limbeck and Malassey).

Cadwalader has demonstrated the presence of nucleated red corpuscles even in mild cases of plumbism; taken alone the presence of nucleated reds does not materially affect prognosis. In a recent fatal case in our hospital we found with abundant basophilic bodies a red count below 1,000,000 and hemoglobin 20.

Grawitz, in 1889, called attention to the presence of basophilic bodies in the erythrocytes with lead poisoning. The detection of *basophilic bodies* is of some importance for prognosis; more important is the fact that it makes the early recognition of the disease possible in lead workers who are watched.

Schmidt contends that 100 basophilic bodies in 1,000,000 erythrocytes demands removal from lead. Grawitz holds that all poisoned with lead show basophilic erythrocytes and that this fact is of the utmost importance for diagnosis and prognosis. Naegeli has seen cases of severe poisoning in which there has been lead in the urine and "marked blue line" without basophilic bodies. The presence of basophilic bodies one day may be followed by their absence the next, and during several subsequent days.

In the present state of our hematologic knowledge we must conclude that while basophilic bodies are present at some time, and usually early, neither their number nor their presence are to be depended upon for prognosis alone; the low erythrocyte count, the presence of *large* numbers of normoblasts, the positive evidences of hemolysis and morphologic change are more dependable when coupled with the clinical picture than the consideration of a single blood change.

Leukocytosis is usual, and with the grave anemias the count is high—at times there is myelocytosis. *The lower the red count with involvement of the central nervous system, delirium, encephalopathies and nephropathies, the worse the outlook. Extreme myasthenia* in these cases often precedes death.

Subacute cases in which there has been sudden poisoning and in which there is daily accession, have been associated with marked hemolysis, low counts and death. My last cases, two brothers, were brought to the hospital from the country where during a number of months they drank cider which was drawn through a corroded lead pipe. Both showed marked anemia and basophilia, one was myasthenic with marked encephalopathy including continuous delirium. He died without showing regeneration, while his brother recovered and with a low blood state, promptly improved. The initial blood picture in these cases was not materially different.

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(f) Saturnine Arteriosclerosis

I have separately considered the influence of lead on the arterial tree and the arteriosclerotic changes resulting (See Arteriosclerosis and Blood Pressure Study), also the influence of lead on gout (See Gout).

Advanced and chronic cases show arteriosclerosis disseminated and a hypertensive condition with aortic lesions and high pulse amplitude. In most of these, there is also interstitial change in the kidneys. Once established, the arteriosclerosis remains though in young subjects, under favorable conditions and treatment, it may not advance. When renal lesions are present and the heart is markedly hypertrophied, toxic symptoms may complicate or sudden myocardial changes are responsible for a fatal termination. Limited arteriosclerosis, i. e., even thickening of the arteries without other complications—even with moderate hypertension, may not *per se* shorten life when the patient is removed from the source of poisoning.

(g) Saturnine Nephropathy

Chronic Interstitial Nephritis

Lead is a frequent factor in producing chronic renal change. It is never in such cases, dissociated from arteriosclerosis; in fact the arterial degeneration of the renal vessels and ultimate connective tissue proliferation with marked hypertension are the leading accompaniments of saturnine nephropathy—usually there is a complete picture of chronic interstitial nephritis with ventricular hypertrophy.

The reader is referred to Section VI—2—Chronic Interstitial Nephritis—for a fuller consideration of the outcome of chronic kidney changes with lead poisoning.

Moderate changes early recognized, without marked or advanced cardiovascular lesions and removal from the poison often remain stationary. The chronic and advanced nephropathies are among the most serious of all lesions and do not yield to treatment, though they too may remain stationary under favorable conditions during many years. The cases with degenerative blood changes, myocardial lesions and coronary or cerebral complications (hemorrhage, miliary aneurism, vascular spasm, thrombosis, uremia) are always life-threatening.

Wickham Legg reports 264 cases of lead poisoning with 32 deaths from some form of encephalopathy; in 43 there was nephritis, in 47 cerebral apoplexy, in 43 paralysis, 38 were tuberculous and 40 died of pneumonia. Among the other causes of death were heart lesions, aneurism, and in 44, "lead poisoning" (probably without evident complication) was given as the cause of death.

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5. Arsenical Poisoning

Acute Arsenical Poisoning

Acute arsenical poisoning interests us only in this work as it leads to symptoms after the initial features have passed and there are evidences of peripheral neuritis, usually multiple or degenerative changes of the liver and other organs which may prove serious. The peripheral polyneuritides associated with arsenical poisoning are separately considered (See Multiple Neuritis).

The poisoning may lead to *arsenical tabes* in which there are motor and sensory symptoms, absence of patella tendon reflex and ataxia, resembling true tabes. Such symptoms with ocular manifestations or more pronounced evidences of polyneuritis with ocular disturbances may follow the use of salvarsan.

Prognosis.—The prognosis of most peripheral disturbances and ocular changes following acute arsencial poisoning is good. Recovery is often slow, but in the end the majority recover with occasional sensory remnants.

Chronic Arsenical Poisoning

Arsenical poisoning follows the use of many articles in domestic use which contain arsenic. Wall paper, (green coloring mainly) has been proven by Gmelin (1839), Basedow (1846) and later Draper, Wood and others to be a source of danger. Articles of clothing, playing cards, carpets, rugs, furs, foods and adulterated drugs (bismuth) have caused isolated arsenical poisoning.

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I have seen a number of cases in which the long-continued use of arsenic for medicinal purposes as a tonic, also for psoriasis, has led to chronic poisoning. One case was reported to me in which an arsenic-charged fluid in the dissecting room used to prepare and preserve material led to alarming symptoms, hyperesthesias and motor insufficiencies. Arsenic eaters (mountain climbers) may develop chronic poisoning.

Prognosis.—The prognosis of most chronic arsenical poisonings is good. After the withdrawal of the drug and rational treatment the sensory, motor and gastro-intestinal symptoms gradually disappear. Paresthesia and anesthesia with slight motor remnant of peripheral neuritis may continue during several months, but cure is the rule. In old subjects who are slowly poisoned I have seen some symptoms of neuritis remain throughout life. If the cord degeneration in any case is far advanced there will be persisting symptoms.

Skin Changes.—The skin changes following excessive sweating (hyperidrosis), maceration with ultimate exfoliation may recur during several months; painful neuralgia or symptoms resembling erythromalalgia are not infrequent. Most of these conditions are accompaniments of arsenical neuritis as is also the characteristic arsenical herpetiform eruption. In chronic cases, the *pigmentation* and *keratosis* may remain permanent and final epithelial thickening (localized) develops. In most cases pigmentation gradually disappears after the supply of arsenic has been cut off. *The leading manifestations of chronic arsenical poisoning are referable to the peripheral nerves and cord.*

Prognosis.—The prognosis is good (See Peripheral Neuritis and Peripheral Paralysis—Section VII).

Accompanying Conditions.—*The associated atrophy* may continue troublesome during discouragingly long periods, but finally there is in most cases gradual return to an approximately normal condition. The *knee jerk* may remain blunted during years or may never reappear; normal reflex is the rule after reasonable periods. In cases which have been undetected during long periods in which arsenic is added from day to day, the condition may be one of extreme weakness with *marked anemia* and *final cachexia.* In one of my cases due to wall paper, *nephritis* developed with *duodenal ulcer,* death resulted from *subphrenic abscess following perforation.*

Psychic disturbances are frequent in the chronic and more severe types; *dementia* is rare but it may develop. The leading symptoms referable to the brain are *amnesia* (forgetfulness), *mental lethargy,* and occasionally *hallucinations.* With psychic symptoms the prognosis is graver than without them. *Ocular lesions* have increased since the introduction of salvarsan and its use for the intensive treatment of syphilis—amblyopia, amaurosis and opacities of the crystalline lens.

Prognosis.—Death due directly to chronic arsenical poisoning is rare and need not be expected unless there are grave complications.

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6. Mercurial Poisoning

Occupational Influence.—Chronic mercurial poisoning is exceedingly rare in the United States. The chief industries which lead to the poisoning are mining and smelting of mercury, the manufacture of thermometers and barometers, instruments of precision in which mercury is used, the production of mercury salts by chemists and the manufacture of felt hats. Occasionally in practice the long-continued and careless use of mercury for medicinal purposes leads to chronic poisoning. Poisoning among miners and workmen is encouraged by carelessness, poor ventilation and lack of cleanliness.

Prognostic Symptoms.—*Stomatitis* with *degeneration of the teeth, extensive ulceration of the gums and buccal mucosa* and *occasional caries of the jaw are the leading early symptoms.* With these symptoms early or later, *gastro-intestinal symptoms* and a *characteristic cachexia* (*cachexia mercurialis*—von Mehring u. Krehl) develop with a peculiar bluish gray or ashen color of the face. The leading and often persistent symptoms are *tremor, erethism* (marked irritability) and *insomnia.* These latter symptoms when coupled with psychic disturbances—mania, hallucinations or mental torpor—brand the case as serious. In grave cases the tremor may be universal; it remains uncontrolled, and is associated with characteristic cachexia and anemia; it continues until death. *Mercurial neuritis* is an occasional accompaniment; *per se* it does not add to the danger.

In the extreme cases the symptoms which threaten life are the uncontrolled *cachexia, anemia, tremor, diarrhea and extreme asthenia.*

Moderate albuminuria in cases which do not present malignant features is not unfavorable. Most chronic cases make satisfactory recoveries unless the poisoning has continued uncontrolled and has been neglected too long.

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7. Carbon Monoxid Poisoning

Illuminating gas poisoning is never anything but a serious incident. It may be acute, or in occasional cases there may be the inhalation of a small quantity of gas due to a continuous small leak which causes positive, but mild and chronic discomfort. In these latter cases, headache, nausea, anorexia, giddiness, somnolence and dyspnea with some cyanosis in the more severe cases, are the leading symptoms. Removal from the gas promptly leads to permanent recovery. The prognosis is less favorable if mental or peripheral symptoms exist.

In *acute poisoning* unless relief is prompt and an abundant supply of oxygen (fresh air) supplied, or if the victim remain in the vitiated atmosphere, the prognosis is absolutely bad.

Symptoms.—*Loss of consciousness, with the congested face, irregular respiration, subnormal temperature* and *disorganized blood* are among the unfavorable symptoms. *Coma* may continue during prolonged periods and yet recovery may follow.

The *blood picture* is characteristic. The degeneration or dissolution of the red blood corpuscle in profound poisoning is prompt; there is concentration of the blood, (polycythemia—polyglobulia) the carbon monoxid combines with the hemoglobin for which it has a strong affinity, and makes the latter useless as an oxygen carrier. Death results therefore from asphyxia. If there is marked leukocytosis the prognosis is bad. There is always some increase of polymorphonuclear cells (Gilman Thompson).

Prognostic Factors.—The dangers from both coal gas and water gas are greater in proportion to the amount of carbon monoxid contained in the atmosphere breathed. An atmosphere which contains one per cent of carbon monoxid breathed during a considerable period proves fatal; if the per cent were larger, death would result correspondingly sooner. Coal gas contains from 4 to 8 per cent of carbon monoxid, while water gas contains between 35 and 45 per cent (40 per cent average). The dangers are not always ended with the disappearance of the acute symptoms, for purpuric conditions, hematogenous jaundice, lesions including bullous eruptions (pemphigus), bed sores and grave central and peripheral disturbances may follow days or weeks after the initial poisoning.

Naturally the great factor in prognosis is the *early discovery of the poisoned subject and immediate treatment.* It is not unusual for sudden death to follow return of consciousness.

Complications.—*Focal softening of the lenticular nucleus or other portions of the brain* have been found post mortem (Poetchen). Multiple neuritis and neurosis (psychoneuroses) are not infrequent sequelae in cases which live beyond the acute period (Oppenheim, Lippmann, Stierlin).

Bronchopneumonia occasionally complicates recovery; if extensive, with high fever, the prognosis is bad. The sequelae referable to the lung

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(pneumonia) may cause death early, i. e., within the first ten days following the poisoning, or several weeks may lapse before the lungs are attacked.

Arhythmias and cardiac weakness may follow or accompany the acute symptoms. In some cases the symptoms resemble *Landry's paralysis;* there is *ascending motor paralysis* and death may follow from *respiratory or cardiac involvement.*

Chorea, tremor, scanning speech and *involuntary discharge of urine may develop* (Edsall). *Symptoms of multiple sclerosis* have developed, as have also *ocular symptoms* including transitory blindness, also *aural symptoms*—tinnitus and deafness.

Prognosis.—In offering prognosis it must be remembered that any of the above mentioned sequelae may develop long after (several weeks) the subsidence of the acute symptoms. Patients may die months after the poisoning from any one of the sequelae mentioned or they may gradually lift themselves back to comparative health.

Patients who develop *psychic disturbances* (dementia) which continue uninfluenced during several months are not likely to recover completely. Of the cases promptly treated 80 per cent live. Of the 20 per cent who die a number yield to complications. Young subjects offer a more favorable prognosis than do the aged.

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8. Pellagra

(*Maidismus*)

Pellagra is a disease of *unknown origin* which is as a rule chronic, but which may be acute; it is associated with early *gastro-intestinal symptoms, cutaneous lesions* (*early erythema*), *marked nervous manifestations* including *great unrest, mental disturbance, depression, suicidal mania, convulsive movements, contractures and paralyses—trophoneuroses* and *characteristic cachexia* in the terminal stages.

Geographical Distribution.—The disease is more prevalent in Southern Europe, Italy and Roumania than on the western continent, though it is at present more frequent in the United States than formerly. It is

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found in country districts oftener than in the city. In central New York it was never known to exist until within the past three years. I know of two deaths, both in country districts, one of which suicided after about fourteen months of continuous symptoms. The other ran a more rapid course to a natural death from asthenia. Neither of these patients ate corn; they were widely separated.

Etiology.—There is no positive proof that the disease is a food intoxication, neither has the recent suggestion of Sambon been accepted by the profession that it is due to an infection of protozoan origin transmitted by sand flies (Genus Simulium).

There is no proof of the contagious character of the disease. The literature of pellagra has grown enormously, but after its thorough review we do not feel that there are any data which establish its etiology beyond doubt.

We have not yet been able to divorce ourselves from the suspicion of the pathogenic influence of maize (spoiled corn or corn products) in the causation of the disease but there are innumerable cases in which corn products have never been used.

Sambon's contention, above mentioned, that the Simulium reptans (sand fly) carries an infecting protozoa has been surrendered; the Thompson-McFadden Commission has pretty thoroughly weakened that theory. Jennings and King after considering insects as a factor in pellagra and the Thompson-McFadden Commission throw a suspicion upon the stable fly (Stomoxys calcitrans) as the carrier of the infection. The entire question of etiology must remain *sub judice* until more convincing proof is offered.

Niles, who has had an enormous experience with pellagra, basing his conclusions on the treatment of over six hundred cases admits that "the etiology of pellagra is unknown."

Prognostic Symptoms and Factors.—The symptoms of pellagra are usually typical, though there have been no characteristic anatomic lesions to brand the disease save as they are found in the skin and rest upon a fundament of trophoneurosis "similar to the degenerations incident to senility" (Niles).

The leading symptoms and factors which influence prognosis are:

(a) Habits (including diet)
(b) Location
(c) Course (acute, subacute, chronic)
(d) Age, race, sex
(e) Gastro-intestinal symptoms
(f) Skin lesions
(g) Psychic disturbances
(h) Central and peripheral lesions of the nervous system.

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(a) Habits

Intelligent living favors pellagrins very materially; in the present state of our knowledge *corn* should be interdicted—at any rate it should be fresh and "should not have undergone heating" (Niles).

In countries where pellagra is endemic there is no doubt of the baneful effect of alcohol. The increase of the disease in Italy (1908-1911) over a preceding equal period is in all probability due to the abuse of alcohol. In all cases, alcohol increases the psychoses.

Pellagrins in order to improve must take advantage of right living, eating, and drinking; their environment exerts an enormous influence on the course of the disease. *Heat* provokes the skin lesions and aggravates subjective symptoms of irritation. *Direct sun rays* are detrimental, as is also excessive heat from stoves or furnaces. *Hot weather invites pellagra;* it is less prevalent or troublesome during the winter months or in a cool atmosphere.

(b) Location

In countries where pellagra has been endemic during long periods the prognosis seems more favorable than in America. This is particularly true of Spain and some parts of Italy where the endemic was widespread, early and severe; later there was a marked drop in the severity of the disease and its incidence. All agree that the disease as seen in the United States offers a graver prognosis than in Europe. The death rate in America varies between 25 and 65 per cent. In Italy and Spain the mortality at times falls to 4 per cent.

(c) Course

Acute and Subacute Cases.—The acute cases with *typhoid condition,* high temperature, rapid pulse and delirium, intestinal symptoms (diarrhea and vomiting) are exceedingly grave. They may die in the course of a few days or weeks and demand differentiation from typhoid fever. In this type as well as with the subacute, *deep invasion of the sensorium* is always of serious significance.

Chronic Cases.—The prognosis of the chronic cases largely depends upon many separate factors including habits, environment, age and symptoms specially considered. In all of these cases rational and intelligent treatment and persistence, materially improve the chances of the patient.

(d) Age, Race, Sex

Age.—Most cases are found during the active years of life (18 to 45). Young subjects offer a better prognosis than do those beyond 50.

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In all, the factors above mentioned (particularly habits—alcohol, environment, etc.) remain powerful.

Race.—The *negro* is more susceptible than the white but under the same conditions the prognosis is not materially different.

Sex.—Women are more frequent victims than are men.

(e) Gastro-Intestinal Symptoms

In chronic or acute cases, persistent gastro-intestinal symptoms—diarrhea, vomiting, anorexia, ulcerative or catarrhal gingivitis, glossitis and stomatitis—and persistent abdominal pain add to the extreme exhaustion and lead to such weakness as we often find associated with cachexia. The dryness of the mouth and glazed tongue with dysphagia in my case, which finally suicided, threatened life during several weeks. Progressive cachexia and persistent diarrhea are always grave.

(f) Skin Lesions

Erythema and bullous eruptions with persistent moisture are evidences of severe disturbance. Moist eruptions have been noted by most observers in the most threatening cases *Symmetry of lesions*, particularly of the forearms, is striking but is of no prognostic significance. Skin lesions should be considered in connection with the other features for prognosis, and not alone.

(g) Psychic Disturbances

The *deeper and more persistent the psychic manifestations of toxemia the worse is the prognosis.*

Mania with the refusal of food and gastro-intestinal symptoms threatened my case during several weeks, during which a cachectic condition developed, from which the patient finally rallied; there was a manic-depression which was never relieved and which led to suicide. Mental alienation demanding removal to a state institution is not uncommon. The prognosis in those committed to public asylums is very bad.

Conclusions.—*It may be safely concluded that the most serious cases are those with profound mental disturbances in which there are also gastro-intestinal symptoms which lead to cachexia and marasmus.*

(h) Central and Peripheral Lesions of the Nervous System

There are cases in which, besides psychic disturbances there are symptoms which can only be explained on the basis of *organic change in the central or peripheral nervous system.* These refer to the cord, in which there is *sphincter involvement* with *blunted deep and superficial reflexes* and *spastic paralysis*, or there are symptoms of *peripheral neuritis.*

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Cases in which these lesions are not deep-seated and are without profound psychoses, the prognosis is not necessarily bad. Niles says: "If the patient is under 50, and has sufficient intelligence and perseverance to adhere to a fixed line of treatment and will faithfully coöperate with the physician, a permanent cure may be expected in the majority of cases."

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9. Beriberi

(*Kakke*)

Symptoms.—Beriberi, or kakke, is a *polyneuritis* associated with fever, in some cases edema or anasarca, and in the subacute and chronic types more or less muscular degeneration causing atrophy.

Etiology.—The disease is due in all likelihood to the eating of *polished rice.* The disease is invited by faulty housing and is frequent in barracks, asylums, on shipboard, in prisons—wherever people are massed in unsanitary quarters among whom polished rice furnishes the larger portion of sustenance. The phosphorus compounds of the pericarp are removed in the process of polishing.

Most cases which come to America are imported from India, China, Japan or from South and Central America. The cases which are found in America are mainly those which have lived through the early stages and present with the clinical picture of multiple neuritis fully established. The number of beriberi patients among the Japanese during the Japanese-Russian war was astounding (over 50,000). Many cases are complicated with *intestinal parasites.*

Wright believes that the disease is positively infectious, "due to a specific organism not yet certainly determined; the organism is not one whose special habitat is any food such as fish or rice, but one that may nevertheless be ingested in any food and drink accidentally contaminated."

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Tsuzuki has (he claims) isolated a germ from the urine and feces of beriberi patients; a diplococcus which in inoculation experiments has reproduced the symptoms of the disease. At present, the consensus of opinion is in favor of a faulty dietary as the etiologic factor.

Forms of the Dieease.—The forms accepted as representing the disease are conceded by clinicians to be the following.

(a) *Incomplete or rudimentary form*
(b) *The atrophic form*
(c) *The wet form*
(d) *The cardiac or pernicious form.*

(a) Incomplete or Rudimentary Form.—Relapses are frequent in the incomplete or rudimentary form. The patient usually recovers after a catarrhal period which is associated with and followed by pains and marked myasthenia with some paresthesia in the legs and edema—not great, as a rule. Respiratory embarrassment, rapid heart and extreme mental and physical exhaustion gradually improve in from a few days to as many months. With the return of warm weather the exacerbations renew the original symptoms in many cases.

(b) Atrophic Form.—With the atrophic form there are marked and persisting symptoms of polyneuritis. The loss of motor power of the legs is prompt and the arms are usually involved—true quadriplegic paralysis (multiple neuritis). The atrophy of the muscles is marked. The face is also involved.

(c) Wet Form.—The wet form—dropsical form—is associated with general edema, including dropsies of the serous cavities. The cardio-respiratory symptoms are more prominent than is the atrophy. With the disappearance of the dropsy the extent of atrophy is apparent.

(d) Cardiac or Pernicious Form.—The cardiac or pernicious form represents the most serious type of the disease. In these cases there is often acute cardiac dilatation, myocardial degeneration or weakness. It may complicate the other forms, and either independent or in combination with the rudimentary or wet form, it may lead to death within a day or two.

The *mortality* varies from a comparatively insignificant percentage to a high figure. Thus Osler places the mortality "from 2 or 3 per cent to 40 or 50 per cent among the coolies in certain of the settlements of the Malay Archipelago." The average mortality of cases which go beyond the acute stage is 20 per cent.

In some the course is acute, the onset sudden with gastro-intestinal symptoms, prompt heart weakness, sensory and motor paralysis, pulmonary edema and death. These are the acute *pernicious cases of Wright.* They all die within a few days.

Our experience with beriberi is so limited in the inland cities of the

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United States that we are dependent entirely for our data upon the study of its literature. The severe polyneuritides which live often leave remnants which never entirely disappear in individual cases.

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10. Food Poisoning

Ptomain and Leukomain Poisoning

Ptomain poisoning depends upon the putrefaction of food in which alkaloidal substances are formed.

Leukomain poisoning depends upon the development of animal poisons in the body, during life.

Food poisons may be either *endogenous*, when, without added contamination the poisonous element is *always* present, or *exogenous* when the poison is accidentally present or *acquired*. The majority of food poisons are exogenous. Epidemics of food poisoning from bacterial contamination are frequent, and usually offer a fair prognosis. Poisoning of severe types may follow the eating of tainted meats or meat products.

Bacterial Invasion of Meats.—The bacterial invasion of meats (colon bacillus, paratyphoid or intermediate bacilli) may lead to grave symptoms within a limited time after eating the contaminated meat, and gastro-intestinal and cardiovascular symptoms with collapse may threaten life. *Collapse with symptoms of cholera, muscular cramps, concentrated blood, cyanosis,* may lead to death in two or more hours, or the patient may gradually rally to remain exhausted during a number of days or weeks.

Contaminated sausage or pork, with the *Bacillus enteritidis* of Gaertner, may cause death in a few days after symptoms of gastro-enteritis, collapse with thin small pulse. Recovery from meat poisoning is the rule, but there are separate poisonings in which many victims are claimed.

In America *veal contamination* is a frequent cause of gastro-intestinal symptoms; while the pains are often severe and collapse frequent, most patients recover. When the meat has *undergone putrefaction* the alkaloids (cadaverin, sepsin and putrescin) are present, and the poisoning

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may prove severe and threatening. The resistance of the patient is often taxed and proves a valuable guide in giving a forecast. Many of these patients may fall into extreme conditions of weakness from which recovery is finally slow, but full.

The poisonings due to milk products, i.e., *milk, cheese, custard* and *ice cream,* are often grave but rarely lead to death. The colic, with gastro-intestinal symptoms, vomiting, diarrhea, exhaustion, rapid pulse, may continue during from one to four or five days. I have rarely lost a patient from this form of poisoning. Weak subjects, children, the sick who are poisoned while passing through acute or chronic illness are bad subjects and a few of these die as the direct result of the added insult. Many of these cases are examples of *tyrotoxicon poisoning.*

Poisoning from fish, also shell fish including *oysters, clams* and *mussel* cause gastro-intestinal symptoms and extreme heart weakness in occasional cases—but recovery is the rule.

Conclusions.—*The contamination of all kinds of food by poisons or bacteria is possible;* each case demands separate consideration; but few who are attended and receive rigorous treatment early will lose their lives, though many make very slow recoveries and the weak may continue below par.

Whatever the source of infected food, it should be remembered that the effect is dependent upon the presence of a specific germ and its toxin, an organic chemical poison of basic nature. Different patients are differently affected during the same poisoning; much often depends upon the prompt emptying of the stomach and intestinal tract, much upon inherent strength and resistance and on the amount and nature of the ptomain taken. Free vomiting and diarrhea early without collapse are favorable. Grave poisoning often develops from twenty-four to forty hours after taking the food.

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Section XII

Diseases Due to Physical Agents

1. Sunstroke

(*Heatstroke, Insolation*)

With periods of long-continued and inordinate heat and exhausting humidity, sunstroke is relatively frequent in the Northern States, particularly in large cities along or near the Atlantic Coast (New York, Philadelphia, etc.) in those who are exposed to the sun or who work in close quarters, in shops, under tin roofs, in engine rooms, among stokers on ocean steamers, also farm hands and diggers.

Contributing Factors.—*Plethora* and *alcoholism* predispose to sunstroke and thermic fever.

Dangers.—The dangers from sunstroke are either (a) *immediate* or (b) *remote.*

(a) Immediate Dangers.—*Sudden vertigo* before marked rise of temperature in workmen on roofs or elevations may lead to fatal accidents or injuries.

Hyperpyrexia is at once the most dangerous and life-threatening symptom. The relief of hyperpyrexia depends largely upon early, prompt and radical treatment. Hyperpyrexia (106°-108° F.) while always serious, is by no means fatal. I have in hospital practice repeatedly saved such cases by energetic and persistent hydrotherapy.

Hyperpyrexia, which refuses to yield after a reasonable period of treatment *with deep coma*, at first full tense pulse, then small rapid pulse, is unfavorable. *Hyperpyrexia with convulsions and persistent coma* is also grave. *Hyperpyrexia during a limited period with profuse perspiration* and but little conjunctival engorgement, few cerebral symptoms after the first two hours is a favorable combination.

Irregular respiration (*Cheyne-Stokes*), hurried respiration, halting or abnormally slow breathing, are all unfavorable—more serious when found in alcoholics and beer drinkers and with chronic nephritis or arterial change.

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Deep coma persisting with or without hyperthermia during unreasonable periods often leads to meningitis and death.

Paralyses, hemiplegia, focal symptoms early are unfavorable. *Persistent delirium and psychopathic types of heat delirium* among stokers may lead to suicide. Cases which begin with pronounced delirium are, as a rule, among the most serious. Symptoms of *meningitis, encephalitis are always of grave moment.* Evidences of invasion of the *pons or medulla* are also serious. *Obese patients* succumb more promptly and easily than do thin subjects. *Once the sensorium begins to clear, the chances of recovery are enormously improved. Relapse into coma and the development of meningitis and encephalitis* are possible—not always fatal.

Atmospheric Influence.—Different seasons offer varying results. Some days of the same season, with equally high temperature, show higher mortality than do other days.

Mortality.—The mortality of sunstroke varies between 5 and 25 per cent, the average in the Eastern States is not far from 12 per cent.

(b) The Remote Dangers.—These include *the tendency to recurrence of hyperpyrexia* on slight cause. These patients are often repeatedly overcome by heat and may develop alarming symptoms, though they rarely die as the direct result of subsequent heatstroke.

Epilepsy has been a remote complication in a small proportion of my cases. *Psychoses* have also followed sunstroke. *Meningitis* has been a late complication in cases after they have lifted themselves out of the primary coma. *Mental lethargy, laziness, loss of memory* and *changed disposition* occasionally persist and follow during long periods, sometimes indefinitely.

Ocular disturbances and deafness, partial or complete, are sequelae which are rebellious to treatment.

Asthenia and *myasthenia* during the summer months are not infrequent sequelae. I have seen two hospital cases in which *peripheral neuritis* complicated convalescence during many months—full recovery never followed in either case.

Thermic Fever

Thermic fever offers a good prognosis in most cases. The symptoms are less deep than with sunstroke; the temperature is more easily controlled; the cerebral manifestations also yield more promptly. Faulty clothing or dress, excessive indulgence in spirits and working during hot weather in unfavorable surroundings are inviting factors. In both sunstroke and thermic fever, degenerative changes in the kidneys and liver as well as myocardial degeneration with meningeal or brain invasion are among the immediate dangers and add to the possibility of remote complications.

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2. Caisson Disease

(*Divers' Paralysis*)

Caisson disease, or divers' paralysis, includes the development of a train of nervous symptoms referable more particularly to the spinal cord —rarely to the brain at the same time—which develop after divers, bridge builders or other workers in caissons under high pressure return to the surface. *Sudden decompression is the important factor in the production of the disease. The increased pressure* leads to characteristic changes which are found in most cases in the brain and cord, at times in the internal organs. In the *acute cases* there is marked hyperemia; in *chronic cases* disorganization of nerve tissue, with consecutive softening is the rule. The latter lesions resemble those found in the advanced types of myelitis, and are incurable.

Thompson says that those who die "comprise" two classes of cases—practically these may be classified as *acute* and *chronic.* The *acute cases* are found "with blood and tissues saturated with gas; in these cases death occurs before organic changes have developed; in the *second, or chronic cases, death results after a protracted course with spinal symptoms; the lesions of disseminated and transverse myelitis with hemorrhages are present.*"

Complications in Chronic Cases.—The complications of these chronic cases include *pneumonia, bed sores, hemorrhagic conditions (purpura), bladder infection, ascending infection of the kidney (pyelitis and pyelonephritis), and at times embolic infarct of the brain and other vital organs.*

Influencing Factors.—Naturally the *amount of pressure, length of exposure and suddenness of return to the surface, are important factors in producing lesions and influencing prognosis.* Because of the increased atmospheric pressure, bubbles of air are forced into the blood, and on reaching the surface these are liberated suddenly. Paul Bert proved that increased atmospheric pressure up to eight atmospheres "is harmless to the circulation and other functions, after which the partial pressure of the oxygen of the absorbed air may exercise toxic effects upon the tissues." *Too rapid decompression is now generally recognized as the cause of the symptoms of divers' paralysis.*

The symptoms develop after the patient leaves the caisson—as a rule, suddenly. The report of Keays which includes the study of 3,692 cases in 10,000 workers which he had the opportunity to study as physician to the Pennsylvania Railroad Tubes, shows but 20 deaths—.54 + per cent.

Cases in which the paralysis—usually referable to the dorsal cord—is of moderate severity, may recover fully after several weeks or a few months. Recovery often follows paralysis which may continue a few days. Hemiplegia often yields but is not as a rule permanent.

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In occasional cases death may promptly follow the initial symptoms. Deep involvement of the sensorium, including coma, delirium and respiratory invasion, is unfavorable.

Allen Starr reports a large experience with caisson disease without a single death. Some patients drag out a wretched existence of chronic invalidism with the unrelieved symptoms of *myelitis, arthritis deformans or aural complications.*

The 20 fatal cases reported by Keays included 6 cases "with pain and prostration," 5 cases showing "symptoms referable to the central nervous system" and 9 cases "showing partial or complete unconsciousness with collapse."

Recovery is often prompt and complete.

Paraplegia may be followed by full or only partial recovery; some of these cases are associated with paralysis of the bladder. *Those cases in which symptoms of myelitis persist, develop the same complications as are found with the ordinary types of transverse and disseminated myelitis* (spastic paraplegia, cystitis, bed sores, pneumonia, and sepsis).

The collective investigation of von Schroetter shows 137 fatal cases of the disease between 1854 and 1897.

Prophylactic measures exert an enormous influence on prognosis.

Keays in his service during the construction of the Pennsylvania tunnels subjected all new caisson workers to a preliminary test. He exposed the workman to thirty pounds of pressure for ninety minutes without exertion of any kind, followed by decompressing the men at the rate of two pounds per minute, i. e., fifteen minutes for the entire time of decompression. If after this test the applicant develops even mild symptoms, insignificant pains, fatigue or weakness in the legs, it may safely be concluded that the workman is below the standard and therefore unfit.

The prognosis is also influenced by *the habits of the workman.*

Those who are below par, muscularly enfeebled, who have arterial, kidney or heart disease, or live in an unfavorable environment, are handicapped and are more likely than those in better general condition to develop the disease.

Frequent shifts and proper feeding after emerging from the caisson are also important in connection with gradual decompression in preventing the development of the disease. *Immediate recompression* has in many cases proved a powerful factor in preventing the full development of the disease.

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3. Mountain Sickness

(*Bergkrankheit, Mal des montagnes*)

Causes and Dangers.—*True mountain sickness,* from which we now exclude "*mountain fever*" (which is usually *typhoid* or *paratyphoid*), and *secondary anemia* (due to *ankylostoma duodenale*), is due to *diminished atmospheric pressure, insufficient oxygen,* to which "all men are subject in an altitude of 16,500 feet and upwards" (Allbutt).

The great danger is due to *cardiac insufficiency* in those who have *myocardial weakness* or *degeneration* with either *hypo-* or *hypertension,* advanced *arteriosclerosis* with or without *coronary narrowing.* In those suffering from *cardiovascular disease,* added *fatigue* and *overeating,* before entering a high altitude, add to the danger of *sudden death.*

Sudden entrance into high altitudes adds materially to the risk of *heart weakness* and *syncope.*

"*Toleration* in the healthy can be easily established when there are compensatory changes in the *blood* and the *readaptation of the respiratory neuromuscular apparatus*" (Allbutt). As the process of acclimatization is established there are likely to be high hemoglobin readings and polycythemia.

The prognosis of mountain sickness in those persons who were *perfectly healthy* before its development is good; the period of acclimatization varies, but is followed by normal function, comfortable breathing, and as above mentioned, blood changes, including increase in the number of erythrocytes and blood coloring matter.

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INDEX

Abscess, perisplenic, 1170.
retropharyngeal, 560.
subphrenic, in cholelithiasis, 730.
of brain. See Brain Abscess.
of kidney, 833.
of liver, in amebic dysentery, 79.
of lung, 386.
in influenza, 127.
in pneumonia, 165.
of spinal cord, associated symptoms of, 914.
course of, 914.
in typhoid fever, 106.
Acetone, test for, Garrod's modification of Rothera's, 1115.
Achondroplasia, 1131.
Achylia gastrica, with pernicious anemia, 522.
stomach contents in, 574-575.
Achylia gastrica nervosa, 618.
Acidosis, in diabetes mellitus, 1115.
chronic, 1116.
in young subjects, 1115.
profound, 1116.
in gastric ulcer, 596.
Acromegaly, and goiter, 1161.
association of, 1161.
characteristic features of, 1161.
course of, 1162.
diagnostic factors of, 1160.
in exophthalmic goiter, 1148.
operative treatment of, 1161.
prognosis of, 1162.
syringomyelia with, 918.
Acroparesthesia, 415.
associated conditions in, 1075.
causative factors in, 1075.
nature and symptoms of, 1074-1075.
Actinomycosis, 301.
alimentary, 302.
cerebral, 302.
character of, 301.
of liver, 302.
of respiratory tract, 302.
of skin, 302.
prognosis of, 303.
with brain tumor, 988.
Acute abdomen, 591-592.
in intestinal obstruction, 635.
Acute indigestion, angina pectoris mistaken for, 458.
arteriosclerosis mistaken for, 409.
Adams-Stokes phenomenon, 29.
Addison's disease, causes of, 263.
duration of, 264.
symptoms of, 263.
Adenia. See Hodgkin's Disease.
Adenitis, in measles, 345.
in scarlet fever, 332.
Adenoids, influence of, on growing child, 299.
pharyngeal, catarrhal condition due to, 358.
Adherent pericardium, associated conditions of, 431-432.
cause of, 430.
prognosis of, 431.
results of, 430-431.
X-ray for, 431.
Adhesions, perigastric, in gastric ulcer, 595.
Adiposis dolorosa, 1078.
Adiposity, in infantilism, simple, 1159.
with genital atrophy, 1159.
Adrenalin, glucosuria produced by, 1107.
in sympathicotonia, 1083.
Adynamia, 634.
Aërophagia, 617.
Ageusia, 870.
Akinesia algera, extreme pain of, 1086-1087.
hysterical, 1017.
mental condition in, 1087.
prognosis of, 1087.
Albuminuria, casts in, 744.
cyclic, 744.
definition of, 741.
false, 742.
febrile, 746.
in typhoid fever, 108.
with non-malignant infections, 746.
following surgical operations, 748.
hematogenous, 742.
in aged and young, 746.
in appendicitis, 654.
in cerebral hemorrhage, 970.
in cholera, 746.
in diphtheria, 139.
in erysipelas, 176.
in influenza, 747.
in nephritis, 741, 743, 793.
in new born infants, 743.
in pneumonia, 160.

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Albuminuria, Leube's rule in, 742.
of nephritis, in typhoid, 108.
of pregnancy, 747, 794.
orthostatic, as suggesting tuberculosis, 745.
continued beyond puberty, 745.
persistent, 745-746.
postural, 744.
provoked by spinal curvature, 745.
parenchymatous, 742.
physiological, 742.
and nephritis, 743.
as misnomer, 743.
prognostic importance of, 741, 748.
recurring, 744.
renal, with casts, 744.
without casts, 744.
toxic, 747.
transitory, 743.
true, 742.
vascular, 742.
with catarrhal influenza, 125-126.
with constitutional diseases, 747.
with glycosuria. See Diabetes mellitus.
with nervous diseases, 747.
with scarlet fever, 746.
with tonsillitis, 747.
Albuminuric retinitis, in chronic interstitial nephritis, 809.
Albumosuria, Bence-Jones, 1134.
detection of, 1134.
myelopathic, 1134.
Alcoholic enteritis, 1181.
Alcoholic gastritis, 571.
Alcoholic meningitis, with alcoholic multiple neuritis, 849.
Alcoholic multiple neuritis, 849.
Alcoholic poisoning, acute, 1179.
in cirrhosis, 694.
Alcoholics, poor surgical subjects, 1181.
Alcoholism, acute poisoning of, associated conditions with, 1179.
causes of death in, 1179-1180.
changes due to, 1180.
symptoms of, 1179.
arteriosclerosis due to, 405-406.
associated with cardiovascular disease, 1179.
associated with chronic laryngitis, 361.
associated with drug habit, 1176.
chronic, associated with chronic laryngitis, 361.
degenerative heart changes in, 1182.
effect of, on circulatory system, 1182.
on gastro-intestinal tract, 1181.
on genito-urinary system, 1182.
on liver, 1182.
on nervous system, 1181.
on respiratory system, 1183.
Korsakoff's psychosis complicating, 1182.
ocular disturbances due to, 1183.
productive and degenerative changes in, 1180.
psychic disturbances due to, 1181.
psychic element as leading factor in, 1180.
Alcoholism, delirium tremens, collapse in, 1184.
duration of, 1184.
infections with, 1184.
prognosis of, 1183.
pulse and temperature in, 1184.
recurrence of, 1183.
symptoms of, 1183.
"wet brain" in, 1184.
epilepsy due to, 1050.
erysipelas in, 174.
exciting factor of disease in, 1178.
formation of habit of, 1176.
general considerations of, 1175.
glucosuria with, 1118.
habit of, 1175.
in syphilis, 41.
in tabes dorsalis, 58.
in tuberculosis, 242.
influencing factors in, early training and discipline, 1177.
heredity, 1177.
intoxication impulse, 1177.
narcotic poisoning, 1178.
periodic drinking, 1177.
personality, 1177.
psychosis, 1178.
time, 1178.
tolerance, 1178.
intestinal changes in, 1181.
loss of will power in, 1175.
pachymeningitis due to, 935.
perverted mind in, 1176.
relapses of, 1178.
supervision of life of patient in, 1178.
with nephritis, 1180.
Aleukemic lymphadenomata, 538.
Algid pernicious malaria, 75.
Alimentary actinomycosis, 302.
Alimentary canal, disturbances of, in typhoid, 101.
Alkaptonuria, 786.
Alopecia, in syphilis, 19.
and atrophic changes, in typhoid fever, 106.
Amaurosis, 857.
Amblyopia, 857.
crossed, 859.
functional, of one eye, 857.
hysterical, 1012.
in epilepsy, 1051.
Amebic dysentery, acute, gangrenous type of, 79.
manifestations of, 78-79.
causes of death in, 80.
chronic, 79.
complications in, 79-80.
manifestations of, 78-79.
mortality from, 80.
myocardial degeneration in, 80.
specific origin of, 78.
symptomatic, 80.
Amenorrhea, in obesity, 1128.
American disease. See Neurasthenia.
Amnesia, in epilepsy, 1053.
in hysteria, 1009.

Digitized by Google

Amorphous urates, precipitation of, 785.
Amygdalitis, 293.
Amyloid degeneration of other organs than liver, 713.
Amyloid kidney, albuminuria of, 741.
  associated diseases of, 814.
  characteristic symptoms of, 814.
  course of, 814.
  origin of, 814.
  urine of, 815.
  vomiting in, 815.
  with operable diseases, 815.
Amyloid liver, primary diseases of, 713.
Amyloid spleen, 1170.
Amyotrophic lateral sclerosis, 890.
Anacidity, 618.
Anadenia gastrica, stomach contents in, 574-575.
Anemia, achylia gastrica with, 522.
  acute (hemorrhagic), 514.
    blood regeneration in, 515-516.
    danger point in, 515.
    due to malignant growths, 515.
    during menstruation, 515.
  Biermer's progressive, 520.
  bothriocephalus, 521.
  chronic (hemorrhagic), blood changes of, 516.
    causes of, 516.
    operable cases of, 517.
  definition of, 514.
  due to malignant growths, 515.
  during menstruation, 515.
  general, 514.
  idiopathic, 520.
  in chronic interstitial nephritis, 809.
  in congenital syphilis, 66.
  in exophthalmic goiter, 1148.
  in malarial cachexia, 76.
  in nephritis, 799-809.
  in trypanosomiasis, 81.
  local, 514.
  neuralgia due to, 838.
  of brain. See Cerebral Anemia.
  of spinal cord. See Spinal Anemia.
  pernicious, acute, 524.
    blood picture of, 519-521.
    blood vessels in, 526.
    causation of, 522.
    cerebral toxemia in, 526.
    complications with, 528.
    diarrhea with, 523.
    glossitis with, 528.
    heart condition in, 526.
    heredity in, 520.
    history of, 520.
    influence on, of splenectomy, 523.
    manner of death from, 528.
    oral sepsis provocative of, 527.
    remissions and periods of latency in, 525.
    retinal hemorrhages with, 527.
    salvarsan for, 528.
    symptoms of, 519.
      Lichtheim, 520, 526.
      nervous, 520, 526.
    temperature in, 527.
Anemia, pernicious, tongue in, 527.
    urine in, 527.
    with fatty liver, 712.
  primary or essential, chlorosis, 517.
    pernicious, 519.
  primary hemolytic, 523.
  saturnine, 1190.
  secondary, to cirrhosis, 693.
  splenic, 1172.
  symptomatic secondary, 514.
  syphilitic, 524.
  with chronic nephritis, 799.
Anesthesia, glucosuria due to, 1110.
  hysterical, 1009-1010.
Aneurism, age and sex considered in, 421.
  death due to, 426.
  definition of, 420.
  dissecting, 421.
  due to infectious processes, 422.
  embolic detachments from walls of, 422.
  greater frequency of, in England and United States than in Europe, 421.
  mycotic-embolic, 422.
  of aorta, descending thoracic and abdominal, 424.
    of ascending portion of arch, 423.
    of descending portion of arch, 424.
    of transverse portion of arch, 423.
  of brain. See Cerebral Aneurism, 997.
  of celiac axis, 425.
  of coronary artery, 425.
  of heart, 467.
  of hepatic artery, 680.
  of pulmonary artery, 425.
  of subclavian artery, 425.
  pathogenic factors of, 421.
  prognosis for life of, 421.
  rupture of wall of, 422.
  stationary, 422.
  syphilitic, 421.
  tendency of, toward progression, 422.
  thrombosis with, 422.
  X-ray examination of, 422.
Angina, Ludwig's, 560.
  pectoris, among professional men, 456.
    and nephritis, 807.
    associated conditions of, 455, 458, 459.
    causes of, 455.
    causes of death from, 458.
    exhausted left ventricle of, 455.
    family tendency to, 456.
    increase of, 456.
    large attack of, 457.
    latent, 455.
    nature of, 454.
    of syphilitic origin, 456.
    prognosis of, 458-459.
    self-cure of, 460.
    small attack of, 457.
    symptoms without actual lesion of, 456.
    uncertainty of, 457.
  pseudo-angina, 456.
  Vincent's, 298.
Angioneural arthroses, 1079.

Digitized by Google

Angioneurotic edema, intermittent dropsy of joints, as atypical types of, 1079.
life-threatening features of, 1076.
Ménière complex due to, 869.
prognosis of, 1076.
symptoms of, 1075-1076.
Ankylostomiasis, 310.
Anorexia, hysterical, 1017.
Anosmia, causes of, 856.
Anterior crural paralysis, 880.
Anthracosis, 380.
Anthrax, character of, 209.
external, malignant anthrax edema, 210.
malignant pustule, 210.
infection of, 209.
internal, gastro-intestinal, 210.
respiratory, 211.
serum for, 211-212.
splenic, 211.
Antitoxin for diphtheria, 142-143-144.
Anuria, 765-766.
calculous, surgical treatment of, 824.
complete, in hydronephrosis, 817.
obstructive, 766.
scarlatinal, 766.
"Anxiety neurosis" of Freud, 1029.
Aortic aneurism, hemoptysis of, 377.
of ascending portion of arch, 423.
of descending portion of arch, 424.
of descending thoracic and abdominal aorta, 424.
of transverse portion of arch, 423.
Aortic insufficiency, associated conditions of, 502.
blood pressure in, 501.
endocarditic form of, 501.
functional form of, 500.
of syphilitic origin, 500.
organic form of, 500.
prognosis of, 501.
pulse in, 502.
Aortic stenosis, 438, 499.
unfavorable cases of, 499.
Aortic tuberculosis, 274.
Aortitis, syphilitic, 27, 423.
in tabes dorsalis, 58.
Aphasia, in cerebral hemorrhage, 969-970.
in cerebral hyperemia, 951.
in encephalitis of children, 979.
optic, 859.
with facial paralysis and hemiplegia, 866.
Apoplectic attack, in cerebral hemorrhage, 963.
Apoplectic habit, 962.
Apoplectiform seizures, in multiple sclerosis of brain and cord, 910.
Apoplexy, and paralysis, table of deaths from, 959.
cerebral, 957.
meningeal, 930.
pulmonary, 378.
Appendicitis, 644.
abnormal position of appendix in, 646.
and typhoid fever, 657.
Appendicitis, catarrhal, apparent improvement of subjective symptoms in, 648-649.
effects of, 649.
fulminating, 649.
nature and symptoms of, 648.
perforation of, 649.
spreading symptoms of, 648.
surgical treatment of, 648.
ulcerative and gangrenous, 649.
chronic, conditions caused by, 655.
danger of intestinal obstruction from, 656.
symptoms of, 656.
complications in, cardiac, 658.
nephritis, 657.
pulmonary, 658.
septic phlebitis, 658.
factors in prognosis of, age, 647.
albuminuria, 654.
effacement of liver dullness, 655.
facies and general appearance, 654.
heart condition, 651.
hiccough, 653.
indicanuria, 654.
leukocytosis, 651.
obstipation, 653.
pain, 653.
physical signs, 654.
pulse, 652.
size and physical signs of tumor, 655.
temperature, 652.
vomiting, 653.
fatty degeneration of liver with, 712.
favorable forecast of surgical treatment for, 644.
fecal concretions in, 646.
fibrinoplastic, 649.
history of, 644.
infectious nature of, 645.
irregular and anomalous course of, 646.
metastatic, 651.
perforative, 650.
fate of pus accumulation in, 651.
general diffuse peritonitis due to, 650.
general septic peritonitis due to, 650.
presence of previous disease in, 651.
retroperitoneal abscesses in, 651.
perforative peritonitis in, prognostic factors of, 652.
peritonitis, acute diffuse, with, 661.
purpuric, 649.
recurring, 655.
reflex symptoms in, 647.
special considerations of, 645.
with rheumatic fever, 289.
Appendix, abnormal position of, 646.
cancer of, 656.
diseases of, 644.
hemorrhage into, in purpura hemorrhagica, 545.
tuberculosis of, 656.
ulcers, typhoid, 650.
Appetite, in diabetes mellitus, 1113.
perverted, of hysteria, 1017.

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Aprosexia, 299.
Arhythmias, auricular fibrillation, 450.
due to depressed conductivity, 447.
due to extrasystoles, 448.
pulsus alternans, 449.
sinus, 447.
Windle's table of, 450.
Arsenical multiple neuritis, 852.
Arsenical poisoning, accompanying conditions of, 1194.
acute, prognosis of, 1193.
symptoms of, 1193.
tabes due to, 1193.
chronic, causes of, 1193.
prognosis of, 1194.
skin changes in, 1194.
encephalitis following, 976.
Arsenical tabes, 1193.
Arterial degeneration, 402.
Arteries, aortic and pulmonary, transposition of, 439.
diseases of, aneurism, 420.
arteriosclerosis, 402.
effect on, of typhoid fever, 95-96.
of spinal cord, changes in, 928.
physiological hyperplasia of intima of, 403.
Arteriocapillary fibrosis, 402.
Arteriorenal disease, 411.
Arteriosclerosis, advanced, 402.
causative factors of, 403.
character of, 402-403.
dictum of Bruce on, 402.
factors in prognosis of, age, 404.
alcohol, 405.
aneurismal dilatation, 413.
blood pressure study, 416.
cardiac asthenia and pulmonary edema, 413.
chemical and toxic, 409.
condition of peripheral arteries, 413.
coronary lesions, 411.
endocardial changes, 413.
gangrene, 414.
heredity, 405.
hypertension, 410.
hypertrophy of left ventricle, 412.
increase of physical signs, 414.
infection, 407.
intermittent claudication, 414.
kidney invasion, 411.
lead poisoning, 406.
mechanical, 409.
myocardial degeneration, 412.
occupation, 407-408.
ocular changes, 415, 418.
overeating, 409.
pulse, 413.
pulse pressure, 417.
thrombosis, 418.
tobacco, 407.
vascular crises, 414.
effects of, 415.
worry and stress, 405.
X-ray, 419.
hemoptysis of, 377.
in aged, 403.
Arteriosclerosis, in chronic nephritis, 802.
in tabes dorsalis, 58.
mortality from, 402.
of hepatic artery, 680.
of syphilitic origin, 67, 404, 405.
period of hypertension in, 403, 410.
appropriate treatment during, 408.
saturnine, 1192.
spinal, 929.
with cholelithiasis, 730.
with cirrhosis, 686.
with paralysis agitans, 1033.
Arteriosclerotic endocarditis, 504.
Arteritis, due to congenital syphilis, 67.
due to syphilis, 26.
blood pressure in, 27.
in tabes dorsalis, 58.
with cerebral syphilis, 40, 43.
Artery, coronary, aneurism of, 425.
pulmonary, aneurism of, 425.
subclavian, aneurism of, 425.
Arthritis, acute, bacteriology of, 279.
and chorea, 1039.
and meningitis, 287.
endocarditis due to, 283.
gonococcus, 192.
in cerebral hemorrhage, 970.
in pneumonia, 167.
in scarlet fever, 332.
myocarditis due to, 285.
with varicella, 342.
Arthritis deformans, absence of symptoms with streptococcus in focus, 1089.
age in, 1090.
atrophic type of, 1091.
beginning at menopause, 1091.
blood and urine in, 1092.
causes of, 1089.
causes of death from, 1092.
climatic conditions in, 1092.
definition and process of, 1088.
etiology and pathology of, 1088.
general condition of patient in, 1091.
Heberden's nodes in, 1091.
hypertrophic, 1091.
hypertrophic hip changes in, 1092.
in hysterical and neurasthenic patients, 1091.
in non-resistant, 1091.
infectious nature of, 1089.
occupation in, 1090.
pathological similarity of, to chronic articular rheumatism, 1088.
prognosis of, 1091-1092.
race in, 1090.
sex in, 1089.
source of infection causing, 1089.
traceable to dental alveoli, 1089.
Arthropathies, in tabes dorsalis, 57.
Arthropathy, hypertrophic pulmonary, 1096.
Ascaris lumbricoides, 309-310.
Aschoff's hemorrhagic erosions in gastric ulcer, 586.

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Ascites, in cancer of liver, 710.
in cirrhosis, 691.
in perihepatitis, 702.
Asiatic cholera, blood picture in, 200.
complications in, 201.
conclusions on, 201.
diarrhea of, 199.
history of, 197-198.
prognosis by stages of, 199.
stages of, cold or algid, 199.
reaction, 200.
symptoms of, 198.
in pernicious malaria, 75.
Astasia-abasia, hysterical, 1016.
Asthenia, due to sunstroke, 1206.
Asthenopia, hysterical, 1012.
Asthma, bronchial. See Bronchial Asthma.
cardiac, 370.
reflex from genito-urinary disturbance, 371.
renal, 370.
thymic, 1164.
vagotonic, 371.
Ataxia, Friedreich's hereditary, symptoms of, in poliomyelitis, 323.
hereditary. See Hereditary Ataxia.
Marie's hereditary, 888.
vasomotor, 1079.
Ataxic paraplegia, associated diseases of, 901.
character of, 901.
course of, 902.
duration of, 902.
forecast of, 902.
Atelectasis, in bronchiectasis, 367.
in bronchitis, 364.
in pleurisy, 391.
Ateliosis, in infantilism, 1159.
Atheromatous degeneration, 402.
Atrophic muscular dystrophy, 897.
Atrophy, genital, in infantilism, 1159.
muscular, in cerebral hemorrhage, 968.
in syringomyelia, 915.
of gall-bladder, due to cholelithisis, 726.
of heart, brown, 454.
starvation, 454.
of liver, acute yellow, differentiated from phosphorus poisoning, 674.
duration of, 675.
nature of, 673.
origin of, 674.
prognosis of, 675.
symptoms of, 673.
optic, 858.
progressive central muscular, 888.
amyotrophic lateral sclerosis, 890.
bulbar paralysis, 891.
duration of, 890.
juvenile or family type of, 890.
spinal, adult type of, 889.
progression of, 889.
remissions of, 890.
reverse in, 889.
symptoms of, 889-890.
unfavorable cases of, 889.
Atrophy, progressive neural muscular, character of, 894.
course of, 894.
senile cerebellar, 1003.
Atropin, vagotonia due to, 1082.
Auditory nerve, paralysis of, 868.
associated symptoms of, 868.
aural vertigo with, 869.
causes of, 868.
degree of deafness in, 868.
invasion of cochlear and facial nerves by, 868.
involvement of vestibular nerve in, 869.
labyrinthine invasion by, 868.
tinnitus aurium with, 868.
Aural disturbances, in diabetes mellitus, 1119.
in neurasthenia, 1030.
Aural vertigo, 869.
apoplectiform type of, 869.
chronic course of, 869.
definition of, 869.
due to angioneurotic edema, 869.
epileptiform seizures in, 869-870.
hemorrhagic cases of, 870.
in neurasthenia and hysteria, 869.
lesions and symptoms of, 869.
prognosis of, 869.
Auricular fibrillation, conclusions of Gossage and Hicks in, 451.
fatal, 450.
favorable cases of, 451.
nature of, 450.
prognostic significance of atropin reaction in, 451.
of digitalis treatment for, 451.

B

Babinski phenomenon, in epilepsy, 1052.
Bacillary dysentery, bacillus of, 193.
character of, 193.
complications in, 195-196.
general considerations of, 193.
incubation period of, 194.
mortality from, 193.
occurrence of, 193.
symptoms of, 194.
Bacilluria, pathogenic bacteria causing, 775.
symptomatic, 774.
Bacterial diseases, anthrax, 209.
Asiatic cholera, 197.
bacillary dysentery, 193.
diphtheria, 134.
epidemic cerebrospinal meningitis, 177.
erysipelas, 173.
glanders, 212.
gonococcus infections, 189.
influenza, 124.
leprosy, 214.
Malta fever, 196.
metastatic parotitis, 300.
paratyphoid, 121.
plague, 201.

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Bacterial diseases, pneumococcus infection, 145.
pyogenic infections, 130.
rheumatic fever, 278.
tetanus, 206.
tonsillitis, 292.
tuberculosis, 216.
typhoid fever, 84, 117.
Bacteriuria. See Bacilluria.
Banti's disease, 1172.
Barlow's disease. See Scorbutus, infantile.
Basedowoid disease, 1149.
Basedow's disease, 1142.
in tabes dorsalis, 58.
Beard's disease. See Neurasthenia.
Bedsores, acute, in cerebral hemorrhage, 966.
in typhoid fever, 106.
Bell's palsy, causes of, 864.
symptoms of, 864.
Beriberi, course of, 1202.
etiology of, 1201.
forms of, atrophic, 1202.
cardiac or pernicious, 1202.
incomplete or rudimentary, 1202.
wet, 1202.
intestinal parasites in, 1201.
mortality from, 1202.
pernicious cases of Wright, 1202.
symptoms of, 1201.
Bile, secretion of, at low pressure, 665.
Bile passages, acute catarrh of (cholangitis, 714.
and gall bladder, diseases of, 718.
Bilharzia hematobia, 316.
Biliary calculus. See Cholelithiasis.
Biliary colic, acute, adhesions due to local inflammation in, 721.
blood picture in, 723.
fever with, 721.
gall-bladder enlargement in, 722.
hyperpyrexia in, 721.
initial attack of, 721.
jaundice with, 721.
liver enlargement in, 722.
prognosis of, 723.
severity of, 722.
splenic enlargement in, 722.
vomiting in, 722.
with relative mitral insufficiency, 720.
with weak myocardium, 720.
x-ray in, 723.
Biliary fistulae, with gall-stones, 730.
Biliary system, 734-735.
Birth palsies, 978.
"Black death," 202.
Black vomit, 347.
Black water disease, 76.
"Bleeders." See Hemophilia.
Bleeding, extragastric, 613.
intragastric, 614.
Blepharospasm, with tic convulsive, 867.
Blindness, bilateral, 857.
due to hemianopia, 859.
complete, 857.
hemianopia, 858.
hysterical, 857, 1012.
Blindness, partial, 857.
unilateral, 857.
Blood and hemapoietic organs, diseases of, anemia, primary or essential, 517.
symptomatic or secondary, 514.
erythremia, 549.
leukemia, 530.
lymphoblastoma, 536.
purpura, 542.
Blood casts, 750.
Blood condition, in Asiatic cholera, 200.
in bronchial asthma, 370.
in cirrhosis, 693.
in diabetes mellitus, 1117.
in epidemic cerebrospinal meningitis, 182.
in epilepsy, 1056.
in erysipelas, 176.
in exophthalmic goiter, 1148.
in genital tuberculosis, 271.
in gonococcus endocarditis, 191.
in hay fever, 358.
in lead poisoning, 1190.
in malaria, 73-74.
in measles, 343.
in paratyphoid, 123.
in pernicious anemia, 519, 521.
in purpura hemorrhagica, 545.
in scarlet fever, 330.
in splenic anemia, 1172.
in trichinosis, 314.
in tuberculosis, 235.
in whooping-cough, 189.
Blood flukes, 316.
Blood poisoning, 130.
Blood pressure, in arteriosclerosis, 416.
in chronic interstitial nephritis, 806
in chronic nephritis, 801.
in myocardial insufficiency, 445.
Blood vessels, in pernicious anemia, 526.
of spinal cord, affections of, 927.
Bones, changes in, due to syphilis, 67.
diseases of, fragilitas ossium, 1097.
hypertrophic pulmonary arthropathy, 1096.
leontiasis ossea, 1095.
osteitis deformans, 1093.
Bothriocephalus latus, 305.
Brachial neuralgia, 843.
Brachial paralysis, anesthesia in, 877.
of circumflex nerve, 878.
Duchenne, 877.
infraclavicular, 877.
motor point in, 877.
musculospiral, 878.
of median nerve, 878.
of posterior thoracic nerve, 877.
prognosis of, 877.
subscapular, 877.
supraclavicular, 876.
ulnar, 879.
Brachial plexus, paralysis of, 875.
due to cervical rib, 876.
involving all nerves, 876.
involving two or more nerves, 876

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Bradycardia, causes of, 511.
false, 511.
hysterical, 1019.
in typhoid fever, 95.
prognosis of, 512.
true, 511.
Brain, actinomycosis of, 302.
anemia of. See Cerebral Anemia.
circulatory disturbances of, abscess of brain (suppurative encephalitis), 980.
anemia, 947.
aneurism. See Cerebral Aneurism.
cerebral hemorrhage, 957.
cerebral paralysis of childhood, 977.
encephalitis, 973.
hyperemia, 949.
occlusion of cerebral vessels, 953.
congestion of. See Cerebral Hyperemia.
cysticercus in, 304.
hydatid disease of, 308.
hyperemia of. See Cerebral Hyperemia.
in measles, 345.
parasites of, 1002.
tumors of, 988.
Brain abscess, bacterial infections causing, 981.
cases of self cure in, 987.
chronic, 987.
conclusions on, 986.
duration of, 986.
extradural pus in, 986.
in amebic dysentery, 80.
infectious origin of, 980.
influenzal, 129.
Jacobson's classification of, metastatic, 984.
otitic, 982.
rhinologic, 985.
traumatic, 981.
location and primary cause of, 981.
lumbar puncture in, 986.
metastatic, infections causing, 985.
location of, 985.
prognosis of, 894.
multiple, 986.
operation for, importance of, 986.
statistics on, 986.
otitic, complications in, 983, 984, 986.
direction of infection in, 982.
with double otitis media suppurativa, 983.
location of, 983.
ophthalmoscopic examination in, 984.
perforation of, 984.
pyemia due to, 984.
single, 983.
symptoms of, focal, 984.
pulse and heart, 984.
various, 984.
prognostic factors in, 986.
rhinologic, development of, 985.
primary causes of, 985.
rupture into lateral ventricle in, 987.
traumatic, causes of, 982.
development of, 981.
location of, 982.
Brain abscess, traumatic, with purulent leptomeningitis, 982.
tuberculous, 981.
without known cause, 985.
"Brain fag," in neurasthenia, 1031.
Brain membranes, diseases of, cerebrospinal meningitis. See Cerebrospinal Meningitis.
leptomeningitis, 937.
pachymeningitis, 934.
syphilitic cerebral meningitis. See Syphilitic Cerebral Meningitis.
tuberculous meningitis. See Tuberculous Meningitis.
Brain parasites, cysticercus cellulosæ, 1002.
echinococcus, 1002.
involvement of cranial nerves by, 1002.
lumbar puncture for, 1002.
symptoms of, 1002.
Brain tumor, 988.
additional considerations of, 998.
age in, 988.
aneurismal dilatation in, 990.
choked disk with, 994-995.
decompression in, 999.
degeneration of, 998.
due to traumatism, 990.
duration of, 999.
heredity in, 990.
hydrocephalus simulating, 943.
localization of, 998.
location of, 990.
lumbar puncture in, 998, 1000.
meningeal hemorrhage in, 1000.
meningitis with, 994.
metastases, 990.
occurrence of, statistics of, 988.
table on, 989.
operation for, factors influencing result of, 1000.
hyperpyrexia following, 1000.
mortality following, 1000.
palliative, 1000.
percentage of recoveries from, 998.
periods of latency in, 999.
pituitary, 1000.
prognostic factors in, 988.
prognostic influence of nature of, 996.
pseudo, 998.
removable, table on, 989.
rupture of, 998.
simulated by hydrocephalus, 943.
social status in, 990.
subcortical, 992.
symptomatic improvement in, 998.
symptoms of, focal, 991.
complex, 991.
hemiplegia, 991.
mental disturbances, 991.
paralysis of two or more cranial nerves, 991.
with spasmodic contractions, 998.
general, constipation, 996.
emaciation, 995.
epileptic seizures, 994.
fever, 993.

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Brain tumor, symptoms of, general, headache, 992.
optic atrophy, 994-995.
optic neuritis, 994-995.
pulse, 993.
psychic, 993.
remission and exacerbation of, 996.
spasms and convulsions, 994.
venous obstruction, 996.
vertigo, 992.
vomiting, 992-993.
weakness, 996.
unilateral, 991.
syphilitic cases of, vomiting in, 993.
tolerance of brain in, 990.
varieties of, 988.
abscess. See Brain Abscess.
aneurism, 997.
carcinomatous deposits, 997.
entozoa, 997.
glioma, 997.
sarcoma, 996.
syphilomata gummata, 997.
tubercle, 996.
with actinomycosis, 988.
without operation, 999.
X-ray in, 999.
Breakbone fever, 356.
Bright's disease, acute, 788.
chronic, 797.
Brill's disease, 120-121.
Brinton's disease, 572.
Bronchi, dilatation of, 366.
diseases of, asthma, 368.
bronchiectasis, 366.
bronchitis, acute, 363.
chronic, 365.
fibrinous, 373.
whooping-cough. See Pertussis.
syphilis of, 33.
Bronchial asthma, age in, 369.
and tuberculosis, 371.
alternating and intercurrent, 372.
antitoxins for, 372.
associated conditions of, 369.
blood picture in, 370.
character of, 368.
"fixed thorax" with emphysema in, 372.
general considerations on, 370.
heredity in, 369.
length of life in, 371.
location and climatic conditions in, 370.
Meltzer's theory of, 368.
occupation considered in, 369.
postural change for, 370.
secondary, 372.
sex in, 369.
sputum of, 368.
symptoms of, 368.
Bronchial catarrh, 364.
dry, of Laennec, 365.
Bronchial lymphadenitis, 265.
Bronchial tuberculosis, 252.
Bronchiectasis, acquired, 366.
associated symptoms of, 367.
atelectasis in, 367.
causes of, 367.
Bronchiectasis, congenital, 366.
development of, 367.
in influenza, 127.
symptoms and course of complications in, 367.
Bronchiolitis, in pneumonia, 165.
Bronchitis, acute, atelectasis with, 364.
primary, 363.
secondary, 364.
symptoms of, 364.
bronchopneumonia with, 364.
capillary, 169.
chronic, associated conditions of, 365-366.
dependent on chronic heart lesions, 365.
effect on, of climatic conditions, 365.
hemoptysis of, 377.
nature of, 365.
purulent, with asthma, 366.
putrid or fetid, 366.
complications in, 364-365.
croupous, 373.
fibrinous, 373.
in influenza, 127.
in measles, 344.
in pneumonia, 165.
in typhoid fever, 98.
with cirrhosis, 693.
with malaria, 77.
Bronchobiliary fistulae, with gall-stones, 730.
Bronchopneumonia, character of, 169.
complications in, 170-171.
significance of, 171-172.
fibrinous, 169.
in measles, 344.
lesions of, in contradistinction to lobar pneumonia, 170.
primary, 169.
with bronchitis, 364.
Bronchorrhea, in pneumonia, 165.
purulent, 366.
types of, 365.
Bruce, dictum of, 402.
Bubonic plague, 203.
Buccal psoriasis, 555.
Bulbar neuritis, acute, 892.
Bulbar paralysis, acute, 892.
asthenic, 893.
degenerative type of, 891.
hemiplegics with, 892.
hemorrhagic cases of, 892.
infantile form of, 892.
myasthenia gravis, 893.
progressive infantile, 892.
pseudo, 893.
symptoms of, 891.
with facial involvement, 865.
Byssinosis, 380.

C

Cachexia, chronic malarial, 76.
due to malaria, 76.
neuralgia due to, 839.

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Cachexia strumipriva, 1155.
Cachexie pachydermique. See Myxedema.
Caisson disease, acute, 1207.
cause of, 1207.
chronic, 1207.
complications in, 1207.
definition of, 1207.
habits of workman in, 1208.
immediate death from, 1208.
influencing factors in, 1207.
prophylactic measures in, 1208.
paralysis, symptoms of, 1207.
paraplegia, 1208.
time of development of, 1207.
Calculi, biliary. See Cholelithiasis.
hepatic. See Cholelithiasis.
pancreatic, 738.
renal, 820.
cystin stones, 821.
large, 821.
multiple, 821.
sand or gravel, 821.
single, without infection, 821.
varieties of, 821.
xanthin stones, 821.
ureteral, 822.
Calculosis, of kidney and ureter, 820.
Calculous anuria, surgical treatment of, 824.
Calculous pyelitis, 831.
Camp fever. See Typhus Fever.
Cancer, cholangitis with, 714.
hysterical, 1017.
metastases to spine and cord due to, 919-920.
of appendix, 656.
of brain, 997.
of esophagus, 567.
of gall-bladder, 717.
of intestines, appearance of subjective symptoms in, 642-643.
cachexia in, 643.
profound blood changes in, 643.
surgical treatment of, 643.
symptoms of, 643.
of kidney, 825.
of liver, acute course of, 711.
encephaloid, 711.
heredity in, 711.
mortality from, 710.
primary, 709.
prognostic factors in, ascites, 710.
edema of extremities, 709.
fever, 710.
jaundice, 709.
spleen, 710.
spontaneous recovery from, 710.
usual secondary nature of, 709.
of pericardium, 434.
of peritoneum, 664.
of spinal cord, 924.
of stomach, age in, 603.
complications in, hypostatic congestion of lung, 612.
metastases, 606, 608.
thrombotic processes, 611.
Cancer of stomach, complications in, tuberculosis, 612.
death rate from, 600.
duration of, 612.
early diagnosis of, its difficulty, 601.
Graefe-Röhmer test for, 601.
importance of, 601.
Leube rule for, 603.
Oppenheimer test for, 601.
for prompt surgical treatment, 608.
Solomon test for, 601.
stomach contents in, 602.
tests for, 601.
by x-ray, 602.
fatality of, 601.
glycyltryptophan test for, 605-606.
general considerations of, 600.
heredity in, 603.
in early life, 603.
incurability of, 608.
infiltrating, without palpable tumor, 608.
latency of, 607.
metastases in, 606, 608.
origin of, in ulcer, 592.
perforation of, 607.
primary, 601.
prognostic significance of leading symptoms of, 604.
race in, 603.
secondary, 603.
sex in, 603.
surgical treatment for, statistics on, 609, 610, 611.
symptoms of, acidity in stomach contents, 605.
blood picture, 606.
disturbance of stomach function, 604.
dropsy, 607.
emaciation, 604.
fever, 606.
hematemesis, 604.
latent, blood picture in, 607.
pain, 604.
ulcerative stomatitis, 607.
urinary, 606.
vomiting, 604.
tryptophan test for, 605-606.
types of, their relative frequency, 603.
pulmonary, 387.
Cancer-free islands, 601.
Cancerous degeneration, in gastric ulcer, 593.
of organ harboring gall-stones, 731.
Cancerous infiltration, in cirrhosis, 687.
Cancrum oris, 555.
in measles, 344.
Capsulitis, 1170.
Caput medusae, in cirrhosis, 689.
Carbon monoxid poisoning, acute, symptoms of, 1196.
chronic, symptoms of, 1196.
complications in, 1196.
prognosis of, 1197.
prognostic factors in, 1196.

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Carbuncles, with diabetes mellitus, 1118.
Carcinoma. See Cancer.
Cardiac asthma, 370.
and obesity, 1127.
influence of, on endocarditis, 489.
Cardiac complications, in appendicitis, 658.
Cardiac neuroses, in neurasthenia, 1029.
Cordiopathia chronica, 477.
Cardiovascular disease, death due to, in alcoholism, 1179.
arteritis, 26.
due to syphilis, aortitis syphilitica, 27.
heart syphilis, 28.
myocarditis, 29.
in scarlet fever, 330.
increase of, in past two decades, 403.
tuberculosis, 274.
Caries of spine, with syringomyelia, 917.
Casts, associated conditions of, 752.
bacterial, 753.
blood, 750.
definition of, 749.
epithelial, 750.
fatty and granular, 751.
fatty or oily, 750.
granular, 749-750.
hyaline, 749, 751.
prognostic significance of, 751.
in albuminuria, 744.
prognostic significance of, 749.
promptly disappearing, 749.
pus, 750.
waxy or amyloid, 750.
Catalepsy, hysterical, 1016.
Catarrh, autumnal, 358.
bronchial, 364.
dry bronchial, of Laennec, 365.
epidemic. See Influenza.
Catarrhal conditions, in typhoid fever, 97.
Catarrhal influenza, 125.
Catarrhal tuberculosis, 250.
Cauda equina, paralysis of, 882.
Cecum mobile, 632.
Celiac disease, 629.
Cerebellar disease, ataxia, 1003.
congenital defects in, 1003.
hemiataxia with, 1004.
hemihypotonia with, 1004.
hemorrhage in, 1003.
invasion of pons by, 1004.
neoplasms, 1003.
nystagmus with, 1004.
of middle peduncle, 1004.
optic neuritis with, 1004.
polioencephalitis hemorrhagica superior, 1004.
reflexes in, 1004.
senile atrophy, 1003.
staggering, 1003.
thrombosis, 1004.
Cerebellar staggering, in Marie's hereditary ataxia, 888.
Cerebral anemia, associated symptoms of, 947.
delirium of inanition in, 948.
due to vascular spasm, 947.
Cerebral anemia, faint spells of, 948.
localized, 947.
paralyses with, 948.
secondary origin of, 947.
secondary to other controllable hemorrhages, 947.
with convulsions, 948.
with lead poisoning, 948.
with unconsciousness, 948.
with uremic intoxication, 948.
Cerebral apoplexy, 957.
Cerebral embolism, and diphtheria, hemiplegia due to, 954.
breaking away from aneurismal coagulum, 954.
chronic, 954.
due to mitral stenosis, 953.
due to septic or malignant endocarditis, 953.
fat, following trauma, 954.
onset of, 954.
origin of, 953.
prognosis of, dependent on area involved, 953.
in thrombosis of pulmonary vein with pneumonia, 954.
recovery from, 954.
seat of, 954.
septic, 954.
with puerperal infection, 954.
Cerebral hemorrhage, age considered in, 959.
and paralysis, table of deaths from, 959.
apoplectic attack in, acute bed-sores in, 966.
Cheyne-Stokes breathing in, 964.
coma in, 963.
duration of, 966.
ophthalmoscopic examination in, 966.
pulse in, 965.
pupils in, 965.
temperature in, 965.
apoplectic habit in, 962.
associated symptoms of, 957.
bed-sores in, 966.
causes of, 958.
Cheyne-Stokes breathing in, 964.
climatic influence in, 962.
coma in, 963.
duration and depth of, 964.
complicating constitutional disease, 958.
due to endocarditis, 960-961.
due to increased blood pressure, 957.
due to syphilis, 960-961.
duration of life in, 972.
following infantile convulsions, 960.
general considerations of, 957.
hemiplegias supposed to be due to, 958.
heredity in, 962.
in early life, 960.
in puerperal period, 961.
influence of special symptoms on prognosis of, apoplectic attack, 963.
period of paralysis, 968.
period of reaction, 967.

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Cerebral hemorrhage, mental conditions following, after coma, 971.
cerebral apoplexy in insane, 972.
change of disposition, 971.
dementia, 971.
in young subjects, 972.
maniacal disturbances, 972.
weakening of intellect, 972.
mortality from, 959-960.
occupation in, 963.
period of paralysis in, albuminuria, 970.
arthritis, 970.
atrophy of muscles, 968.
Babinski phenomenon, 968.
exalted knee reflex, 968.
hemianesthesia, 969.
hemianopsia, 970.
inclusion of medulla oblongata, 970.
posthemiplegic motor complications, 970.
secondary contractures, 968.
transitory cases, 969.
period of reaction in, 967.
aphasia, 969-970.
hemiplegia, 969.
improvement of motor function, 969.
symptoms during, 967.
pneumonia with, 972.
prodromata of, 963.
recurrence of, 972.
rupture in, 957-958.
sex considered in, 962.
spontaneous, 961.
traumatic, 959.
with chronic interstitial nephritis, 958.
Cerebral hyperemia, active, 950.
assumptions in prognosis of, 950.
cases suggesting, due to chronic constipation, 952.
classification of, 949.
due to toxemia, 949, 951.
leading causes of, 950.
merging of forms of, 951.
passive, 950, 951, 952.
pathology of, 949.
prodromal stage of, 952.
prognosis of, 952.
secondary origin of, 949.
soporific, with apoplectiform symptoms, 951.
symptoms of, aphasic, 951.
apoplectiform, 950.
convulsive, 951.
paralytic, 951.
soporific, 951.
with mania, 951.
Cerebral neurasthenia, 1028.
Cerebral paralysis, choreatic paresis with, 980.
of childhood, acute encephalitis of children, 979.
birth palsies, causes of, 978.
Oppenheim-Vogt type of, 978.
symptoms and prognosis of, 978.
differentiation of acquired and congenital, 978.
Cerebral paralysis, of childhood, due to intra-uterine anomalies, arrested development of cortex cerebri, 977.
cysts developed in fetus, 977.
influence of heredity on production of epilepsy after, 977.
prognosis of, 977.
uremic, 764.
Cerebral polioencephalitis, 322.
Cerebral softening, 953.
Cerebral syphilis, 38.
arteritis in, 40, 43.
degeneration of brain tissue in, 40.
deposits in, 42.
epilepsy in, 42.
examination of spinal fluid in, 40.
general considerations of, 39.
globulin reaction in, 40.
gummatous lesions in, 40.
hemiplegia in, 43.
interval between specific infection and development of, 41.
lumbar puncture in, 38.
malignant types of, 41.
meningitis, specific localized with, 42.
paralysis of motor oculi in, 43.
primary, 42.
prognosis of, 41.
relapse of, 41, 43.
secondary, 41.
single gumma in, 42.
specific endarteritis in, 42-43.
Cerebral thrombosis, about an embolus, 956.
anemias and leukemias ending in, 955.
coma with, 956.
due to blood changes and weakened heart, 956.
during puerperal period, 956.
following otitis, 955.
frequency of, 955.
in senile subjects with arteriosclerosis, 956.
multiple "marantic" thrombi, 955.
of small arteries, without symptoms, 956.
pathologic conditions predisposing to, 955.
primary, of longitudinal sinuses, 955.
prognosis of, 956.
seat of, 955.
slow formation of, 955.
symptoms of pseudobulbar paralysis in, 956.
with chronic alcoholism, 956.
with paralysis, 956-957.
with specific endarteritis, 956.
Cerebral toxemia, in pernicious anemia, 526.
Cerebral vessels, occlusion of, by embolism, 953.
by thrombosis, 955.
Cerebral vomiting, 993.
Cerebrospinal meningitis, 932.
epidemic, hydrocephalus due to, 182.

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Cerebrospinal syphilis, hereditary, 37.
Cervical lymphadenitis, 265.
Cervical nerves, paralysis of, hiccough-spasm of diaphragm, 875.
phrenic, 874.
Cervical pachymeningitis, hypertrophic, bladder symptoms in, 933.
prognosis of, 933.
symptoms of, 932.
syphilitic cases of, 933.
Cervical rib, paralysis due to, 876.
sensory and motor disturbances due to, 876.
surgical removal of, 876.
Cervical sympathetic, irritation of, 1082.
paralysis of, 1081.
Cestodes, Bothriocephalus latus, 305.
Tenia echinococcus, 306.
cysts of, 306-307.
in brain, 308.
in heart, 466.
in kidney, 308.
in liver, 307.
in lung, 308.
in other organs, 309.
in spleen, 308.
Tenia mediocanellata, 305.
Tenia saginata, 305.
cysticercus of, 305.
Tenia solium, character of, 304.
cysticercus of, 304-305.
seats of, 304-305.
symptoms of, 304.
Chalicosis, 380.
Charcot, "grande hysterie" of, 1016.
hysterical stigmata of, 1005.
Cheyne-Stokes breathing, in cerebral hemorrhage, 964.
Chicken pox. See Varicella.
Chloroleukemia. See Leukemia, lymphatic.
Chloroma, with lymphatic leukemia, 533.
Chlorosis, blood picture of, 517.
causes of, 518.
chronic, 519.
complications with, 518.
nature of, 514, 517.
oligocythemia with, 518.
subjective symptoms of, 518.
Choked disk, with brain tumor, 994-995.
Cholangitis, acute, 714.
chronic, nature of, 714.
produced by gall-stones, 715.
with cancer, 714.
suppurative, 715.
Cholecystitis, acute, 715.
acute phlegmonous, 717.
chronic, 716.
in typhoid fever, 105.
obliterative, 716.
and cholangitis, 716.
with gangrene, 717.
Cholelithiasis, absence of symptoms in, 718, 728.
acute biliary colic in, adhesions due to local inflammation in, 721.
blood condition of, 723.
Cholelithiasis, acute biliary colic in, enlargement of gall bladder with, 722.
enlargement of liver with, 722.
enlargement of spleen with, 722.
fever with, 721.
hyperpyrexia with, 721.
initial attack of, 721.
jaundice with, 721.
prognosis of, 720.
relative mitral insufficiency in, 720.
severity of, 722.
small stones in intestines in, 723.
vomiting with, 722.
with weak myocardium, 720.
x-ray examination for, 723.
adhesions in, protection offered by, 729.
adhesions of gall bladder and duodenum or pylorus in, 729.
age in, 719.
arteriosclerosis with, 730.
associated infection in, 719, 728.
associated with malignant disease, 719.
associated with metabolic faults, 719.
cancerous degeneration in, 731.
cholesterin, main constituent of, 718.
chronic, adhesions in, 724.
effect on patient, 723.
location of stones in, 723.
prognosis of, 724.
pyloric obstruction in, 724.
secondary changes due to, 724.
with added chronic infection, 730.
complications in, 728.
due to diet, 719.
endocarditis with, 731.
fistulae in, 728.
biliary, 730.
bronchobiliary, 730.
urinary, 730.
frequency of, in internal diseases, 719.
gangrenous gall-bladder in, 728.
hemorrhage in, 732.
interstitial nephritis with, 730.
intestinal obstruction in, 729, 731.
migration of stones into right kidney in, 730.
myocarditis with, 731.
nervous system in, 732.
obstruction of common duct by, "adventitious outlets" for bile in, 725.
ball valve action of stone in, 726.
changes caused by, 725.
complete, 725.
Courvoisier's law, 725.
effect of, on gall-bladder, 725.
liver abscess due to, 726.
partial, 725.
serious complications of, 725.
source of, 725.
ulceration in, 725.
obstruction of cystic duct by, atrophy of gall-bladder with, 726.
dilatation of gall-bladder with, 726.
duration of, 726.
source of, 726.
symptoms of, 726.

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Cholelithiasis, obstruction of hepatic and intra-hepatic ducts by, causation of, 727.
coincident with stones in other passages, 727.
prophylaxis in, 727.
stones in liver substance in, 727.
pancreatic disease with, 731.
passing of stones by rectum in, 729.
perforation of gall-bladder in, 728.
perforation into peritoneum in, 729.
process of, 719.
protective factors in, 728.
sex considered in, 719.
solubility of stones in, 719.
spontaneous solution of, 720.
subphrenic abscess in, 730.
surgery in, 733.
ulceration into portal vein and into hepatic artery in, 730.
vagaries of, 718, 729.
wanderings of stones in, 729.
Cholera asiatica. See Asiatic Cholera.
Cholera morbus, 623.
Cholera nostras, 623.
Cholerine, 200.
Cholesterin, 718.
Chondrodystrophy, fetal, 1131.
Chorea, acute hereditary, 1043.
associated conditions of, grippal infection, 1040.
associated diseases of, arthritis, 1039.
gonorrhea, with endocarditis, 1040.
polyarthritis, with endocarditis, 1040.
purpura rheumatica, 1039.
streptococcus viridans infection, 1039.
tonsillar, 1039.
chronic, 1043.
chronic progressive, 1044.
complications in, cardiac, 1042.
conditions influencing, age, 1038.
heredity, 1038.
moisture and exposure, 1038.
psychic disturbances, 1038.
race, 1038.
sex, 1038.
unhygienic conditions, 1038.
definition of, 1037.
Dubini's, 1046.
electrical, 1046.
endocarditis in, 1042.
endocarditis and rheumatism with, 284.
family, 1044.
foudroyant cases of, 1043.
history of, 1038.
Huntington's, 1044.
in aged, 1043-1044.
latent, 1041.
mortality from, 1043.
myocarditis in, 1042.
nature of, 1037.
problematic nature of, 1037.
prognostic factors in, heart anomalies, 1042.
loss of flesh, 1041.
mental symptoms, 1040.
motor disturbances, 1041.
Chorea, prognostic factors in, muscular weakness, 1041.
ocular errors in, 1040.
sensory disturbances, 1041.
sphincter involvement, 1041.
psychic disturbances in, improvement of, 1042.
recurring, and endocarditis, 1043.
relapse of, 1043.
subacute, 1043.
symptoms of, eosinophilia, 1041.
Chorea gravidarum, 1040.
Chorea minor, 1037.
Choreatic paresis, 980.
Chylous urine, 776.
Chyluria, non-parasitic, 776.
parasitic, 776.
Circulatory disturbances, in typhoid fever, 93.
of lung, congestion, 373.
Circulatory system, diseases of, aneurism, 420.
arteriosclerosis, 402.
congenital defects of heart, defective intraventricular septum, 438.
dextrocardia, 438.
insufficiency and stenosis of mitral and tricuspid valves, 439.
perforate foramen ovale, 438.
stenosis of aortic orifice, 438.
stenosis of pulmonary orifice, 435.
transposition of aorta and pulmonary artery; perforate and premature closure of ductus arteriosus, 439.
endocardial, acute, 468.
chronic, 477.
functional heart disorders, 506.
bradycardia, 511.
neurasthenic state, 512.
palpitation, 507.
tachycardia, paroxysmal, 508.
tachycardia, simple, 510.
gastric, enteroptosis, 579.
myocardial, 441.
aneurism, 467.
chronic insufficiency, 443.
heart weakness due to insufficient exercise, 464.
hypertrophy and dilatation, 460.
inherent muscular weakness, 465.
insufficiencies with anemias, metabolic faults and toxic states, 465.
myocarditis, acute interstitial, 443.
myocarditis, acute purulent, 442.
neoplasms, 465.
parasites, 466.
rupture, 466.
Stokes-Adams disease, 463.
syphilis. See Cardiovascular Disease.
pericardial, adherent pericardium, 430.
hemopericardium, 433.
hydropericardium, 433.
neoplasms, 434.

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Circulatory system, diseases of, pericardial pericardioperitonitis, 432.
pericarditis, 426.
pneumopericardium, 434.
in alcoholism, 1182.
in erysipelas, 175.
in pneumonia, 153.
Circumflex nerve, paralysis of, 878.
Cirrhosis, and nephritis, 685.
biliary, 698.
capsular, 701.
associated symptoms of, 701.
fatal terminations of, 703.
tapping in, 702.
complications with, alcoholic poisoning, 694.
arteriosclerosis, 686.
bronchitis, 693.
cerebral, 695.
coma, 694.
convulsions, 695.
delirium, 694-695.
gout, 695.
invasion of nervous system, 694.
pleurisy, 694.
pneumonia, 694.
progressive lenticular degeneration, 695.
renal insufficiency, 694.
terminal infections, 695.
tuberculosis, 693.
uremia, 694.
Hanot's hypertrophic biliary, 698-699.
Laennec's, duration of, 698.
late operation for, 697.
malarial, cases of, 696.
mortality from, 683.
multilobular, 682.
alcoholic history of, 682.
etiology of, 683.
faulty diet as factor in, 682.
prognostic factors of, 682.
spleen as factor in, 682.
splenectomy for, 682.
obstructive biliary, 698-699.
of liver, chronic gastritis associated with or secondary to, 573.
enlargement of spleen with, 1170.
nature of, 681.
with tuberculosis, 255, 258.
of lung, 379.
of stomach, 572.
pericellular, 701.
pigmented, 696.
hemachromatosis, 696.
prognostic factors of, arteriosclerosis, 686.
cancerous infiltration, 687.
esophageal lesions, 685.
heart condition, 687.
individual symptoms, 687.
intestinal lesions with, 685.
kidney lesions, 685.
latency, 684.
latency and complications, 685.
lesions in other organs, 685.
peritonitis, 686.
Cirrhosis, prognostic factors of, pulmonary tuberculosis with, 686.
stomach lesions with, 685.
progressive, secondary anemia with, 693.
surgical treatment for, 696-697.
symptoms of, ascites, 691.
blood condition, 693.
caput medusae, 689.
change in size of liver, 690.
epistaxis, 690.
facies, 688.
gastro-intestinal, 688.
general dropsy, 691.
heart, 696.
hematemesis, 689.
hematuria, 690.
hemoptysis, 690.
ill defined, 687.
jaundice, 692.
melena, 690.
pulse, 695.
respiration, 696.
skin lesions, 696.
splenic, 689.
temperature, 695.
urinary secretion, 691.
venous obstruction, 688.
weight, 688.
syphilitic, 701.
unilobular, 698.
blood condition in, 700.
causes of, 699.
complications with, 699.
conclusions on, 701.
course of, 700.
general statements on, 698-699.
jaundice in, 700.
joint changes in, 700.
myocardial insufficiency in, 700.
size of spleen in, 700.
urine in, 700.
Claw hand, 879.
Clubbed fingers, 1096.
Cocainism, effects of, 1187.
prognosis of, 1187.
Cochlear nerve, invasion of, in auditory paralysis, 868.
Colitis, acute membranous, secondary, 623.
membranous, in pneumonia, 161.
mucous, infantile, 623.
infectious, 622.
nervous or hysterical, 622.
secondary, 622.
Colitis cystica, 624.
Colles-Baume law, 65.
Colon, dilatation of, 640.
Color perception, faulty, hysterical, 1012.
Coma, in cerebral hemorrhage, 963.
in cerebral thrombosis, 956.
in cirrhosis, 694.
in malarial fever, 75.
Common duct, obstruction of, 725.
occlusion of, 715.
Compensatory hypertension, in chronic nephritis, 802.
Compensatory hypertrophy, 582.

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Compensatory hypertrophy, in chronic nephritis, 797, 802.
Concussion of spine, 1021-1022.
Congested kidney, acute, as secondary condition, 811.
associated with acute infections, 811.
heart lesions provoking, 812.
prognosis of, 812.
chronic, causes of, 812.
due to heart lesions, 812.
condition of urine in, 813.
conditions associated with, 813.
due to local obstruction, 813.
due to pulmonary obstruction, 813.
due to venous stasis, 813.
prognosis of, 813.
Congestion, pulmonary, 373.
of brain. See Cerebral Hyperemia.
of liver, 676.
Conjunctival diphtheria, 138.
Conjunctivitis, in measles, 343.
Constipation, 630.
and hemorrhoids, with obesity, 1127.
atonic form of, due to insufficient expulsive strength, 631.
due to reduced intestinal peristaltic activity, 631.
cathartics for, 633.
causes of, 630-631.
due to cecum mobile, 632.
due to habits, 630, 632.
hysterical, 1017.
in brain tumor, 996.
organic causes of, 631.
spastic, 632.
with neurasthenia, 1031.
Contractures, hysterical, 1014.
Convergent strabismus, 861.
Convulsions, in brain tumor, 994.
in cerebral anemia, 948.
in cirrhosis, 695.
in malarial fever, 75.
infantile. See Infantile Convulsions.
Coronary disease, due to arteriosclerosis, 411.
with chronic nephritis, 802.
Coronary sclerosis, 454.
Coryza. See Rhinitis, Acute Catarrhal.
in congenital syphilis, 66.
Cough, hysterical, 1018.
in pneumonia, 155.
in pulmonary tuberculosis, 229.
Courvoisier's law, 725.
Cranial nerves, paralysis of, abducens, 861.
auditory, 868.
Bell's palsy, 864.
facial, 863.
due to pontine disease, 864.
facial or mimic spasm, 866.
facial hemiatrophy, 863.
glossopharyngeal, 870.
hypoglossal, 873.
motor oculi, 860.
ocular, 860.
ophthalmoplegia, 861.
optic, 857.
pneumogastric, 871.
Cranial nerves, paralysis of, spasm of spinal accessory muscles, 872.
spinal accessory, 871.
tic convulsive, with, 867.
trigeminal, 862.
trochlear, 861.
peripheral paralysis of, olfactory, 856.
Cretinism, congenital, 1155.
prognosis of, 1155.
symptoms of, 1155.
thyroid treatment for, 1156.
due to complete loss of gland function, 1157.
endemic, 1156.
fetal, 1131.
heredity in, 1158.
prognosis of, 1158.
sporadic, 1155.
Cretinoid change. See Myxedema.
Crural neuralgia, 844.
Crural pains, 840.
Cylindroids, 750.
Cystic duct, obstruction of, 726.
Cysticercus. See Cestodes.
Cysticercus cysts, in tumors of spinal cord, 924.
Cystinuria, conditions indicated by, 785.
Cystitis, in typhoid, 109.
Cystoscopic examination, in pyelitis, 832.
Cysts, pancreatic, 738.
renal, 826.
splenic, 1171.

D

Dandy fever, 356.
Deafmutism, due to epidemic cerebrospinal meningitis, 868.
Deafness, 868.
Decubitous ulcers, of esophagus, 564.
Decubitus, in acute myelitis, 905.
Delirium, epileptic, 1053.
in cirrhosis, 695.
of inanition, 948.
Delirium cordis, 510.
Delirium tremens, collapse in, 1184.
duration of, 1184.
infections with, 1184
prognosis of, 1183.
pulse and temperature in, 1184.
recurrence of, 1183.
symptoms of, 1183.
"wet brain" in, 1184.
with alcoholic multiple neuritis, 849.
Dementia, in cerebral hemorrhage, 971.
in epilepsy, 1053.
in paresis, 64.
Dementia paralytica. See Paresis.
Dengue, 356.
Dercum's disease, 1078.
Dextrocardia, 438.
Diabetes, glucosuria and, in exophthalmic goiter, 1147.
in tuberculosis, 242.
neuralgia due to, 839.
Diabètes bronzé, 1107.

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Diabetes insipidus, as incurable complex, 1124.
backache in, 1124.
blood picture in, 1123.
characteristic features of, 1122.
heart and blood pressure in, 1123.
heredity in, 1123.
idiopathic, 1122.
influence of hypophysis in, 1123.
primary, 1124.
quantity of urine secreted in, 1123.
secondary, 1122.
urine in, 1123.
Diabetes mellitus, acute, 1113.
chronic, 1113.
acidosis in, 1115.
and gout, 1119.
aural disturbances in, 1119.
blood condition in, 1117.
carbuncles in, 1118.
emaciation in, 1114.
furuncles in, 1118.
gangrene in, 1118.
hunger in, 1113.
infections complicating, 1117.
mental state in, 1115.
muscular weakness in, 1116.
nervous system in, 1118.
ocular infections with, 1119.
pneumonia with, 1117.
polyuria in, 1114.
pulse and blood pressure in, 1114.
pruritus with, 1118.
relative value for prognosis, of individual symptoms in, 1113.
sexual anomalies in, 1117.
skin lesions in, 1118.
thirst in, 1114.
tuberculosis with, 1118.
urine in, 1116.
eternal vigilance in, 1121.
fasting method of treatment for, 1121.
general considerations of, 1106.
glucosuria in, alimentary, 1108.
due to adrenalin, 1107.
due to disease of hypophysis, 1107.
due to liver disease, 1107.
due to pancreatic disease, 1106.
due to skeletal muscles, proteid and fat, 1108.
due to surgical lesions, 1119.
due to thyroid extract, 1107.
due to traumatism, 1108.
glucosuric condition in, 1106.
impossibility of cure in, 1121.
in infancy and childhood, 1112.
in obese, 1112.
increase of cellular resistance in, 1120.
negative factors in, contagion, 1108.
kidney, 1108.
pancreatic disease with, 1106.
process of, 1106.
prognostic factors in, age, 1110.
control of hyperglycemia, 1111.
heredity, 1110.
race and geographic location, 1111.
sex, 1110.
Diabetes mellitus, relation to, of lactosuria, 1109.
surgery for, 1119.
in presence of acetone or diacetic acid, 1120.
preliminary treatment, 1120.
vulnerability of tissue in, 1118.
with syringomyelia, 917.
Diaphragm, spasm of. See Hiccough.
Diarrhea, acute. See Enteritis, acute.
chronic, 623.
gastrogenic, 624.
gastro-intestinal, 624.
hysterical, 1017.
in pernicious anemia, 523.
in pulmonary tuberculosis, 232.
in typhoid fever, 102.
secondary chronic, primary causes of, 625.
with exophthalmic goiter and Addison's disease, 625.
Diarrhea alba, 629.
Diarrhea chylosa, 629.
Diarrheal diseases, of early childhood, mortality from, 627-628-629.
prophylaxis against, 627.
Schmidt's bile test, 629.
symptoms of, affecting prognosis, 629.
Diazo-reaction, 234.
Dietl's crises, in gastroptosis, 580.
with nephroptosis, 829.
Digestive system, diseases of, appendiceal, appendicitis, 644.
cancer, 656.
tuberculosis, 656.
bile passages and gall-bladder, cholangitis, 714.
cholecystitis, 715.
cholelithiasis, 718.
esophageal, cancer, 567.
dilatation, 568.
diverticula, 569.
esophagitis, 562.
rupture, 568.
spasm and paralysis, 565.
stricture, 566.
gall-bladder, cancer of, 717.
intestinal, cancer and other growths, 642.
celiac disease, 629.
constipation, 630.
diarrheal diseases of early childhood, 627.
dilatation of colon, 640.
diverticulum, 641.
enteritis, acute, 619.
enteritis, chronic, 623.
enteroptosis, 579.
obstruction, 633.
liver, abscess, 704.
acute yellow atrophy, 673.
amyloid, 713.
circulatory disturbances, 676.
cirrhosis, 681.
echinococcus. See Echinococcus disease.

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Digestive system, diseases of, liver, fatty, 712.
jaundice, 664.
neoplasms, 709.
syphilis of. See Syphilis.
tuberculosis of. See Tuberculosis.
mouth, stomatitis, 553.
pancreatic, calculi, 738.
cysts, 738.
hemorrhage, 737.
necrosis, 738.
neoplasms, 739.
pancreatitis, 734.
peritoneal, new growths, 663.
peritonitis, acute diffuse, 659.
peritonitis, chronic, 662.
tuberculosis. See Tuberculosis.
pharyngeal, circulatory anomalies, 559.
pharyngitis, 559.
salivary glands, Mikulicz disease, 557.
mumps. See Parotitis, epidemic.
parotitis, 557.
stomach, cancer of, 600.
dilatation, 576.
gastric and duodenal ulcer, 585.
gastric neuroses, 615.
gastritis, acute, 570.
gastroptosis, 579.
gastrorrhagia, 613.
hematemesis, 613.
pyloric obstruction, 581.
tonsillar. See Infectious Diseases.
syphilis of, 34.
tuberculosis of, 252.
Dilatation of colon, due to gas, 640.
due to organic stricture, 640.
idiopathic, 640.
with solid matter within it, 640.
x-ray in, 640.
of esophagus, 568.
of stomach, acute, 576.
involvement of innervation in, 577.
with pneumonia, 577.
with pneumonia and chronic valvular disease, 577.
atonic, 578.
primary myasthenic, 577.
congenital, 578.
secondary chronic, obstruction as cause of, 578.
tetany in, 579.
Diphtheria, and cerebral embolism, hemiplegia due to, 954.
and hemiplegia, 954.
antitoxin for, blood counts after injection of, 142.
conclusions on, 144.
mortality statistics on, 144.
serum sickness, 142-143.
bacteriology of, 134.
carriers of, 136.
complications in, heart, 139-140.
nephritis, 139.
otitis media suppurativa, 142.
paralysis, 140.
Diphtheria, complications in, parotitis, 142.
pleurisy, 142.
pneumonia, 142.
conjunctival, 138.
endocarditis with, 140.
factors influencing growth of, 135.
history of, 134.
in measles, 345.
in scarlet fever, 329.
laryngeal, 136, 138.
liver and spleen in, 142.
myocarditis in, 139.
nasal, 138.
of vulva, 138.
paralysis in, 140.
asphyxia in, 141.
facial, 865.
glossopharyngeal, 141.
hemiplegia in, 141.
ocular, 141.
of extremities, 141.
pneumogastric, 141.
simple uncomplicated, of soft palate, 141.
von Behring antitoxin for, 141.
pharyngeal, gangrenous, 137.
mild infection without severe general toxemia, 136.
with severe toxemia, 137.
relapses of, 142.
skin, 138.
sudden death from, 140.
vomiting with, 142.
Diphtheritic dysentery, 194.
Diphtheritic enteritis, 621.
Diphtheritic esophagitis, 564.
Diplegia, spastic, 978.
Diplopia, in paralysis of sixth nerve, 861.
Divers' paralysis. See Caisson disease.
Diverticulum, of intestines, 641.
effects of, 642.
false, 641.
true, 641.
"Drop-foot," 881.
Drop wrist, in lead multiple neuritis, 850.
in musculospiral paralysis, 879.
Dropsy, and obesity, 1128.
in chronic interstitial nephritis, 807.
in chronic nephropathies, 800.
in cirrhosis, 691.
in endocarditis, 492, 496.
of gall-bladder, 726.
of joints, intermittent, 1079.
Dubini's disease, 1046.
Duchenne paralysis, 877.
Ductless glands, diseases of, parathyroid, 1165.
pituitary, 1158.
splenic, 1169.
suprarenal, 1163.
thymus, 1163.
thyroid, 1136.
Ductus arteriosus, perforate, and premature closure of, 439.
Duke's disease, 352.

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Duodenal ulcer, alcoholic, 1181.
and gastric, relative frequency of, 587.
due to surface burns, 588.
hyperchlorhydria symptomatic of, 588.
indicanuria in, 588.
perforation of, 590.
subphrenic abscess formed by, 591.
with chronic nephritis, 588.
Duodenitis, acute, 620.
Duodeno-cholangitis, 714.
Duodenum, adhesions of, in cholelithiasis, 729.
Dura mater, inflammation of, 934.
Dysentery, amebic. See Amebic Dysentery.
bacillary, 193.
diphtheritic, 194.
with malaria, 77.
Dyspepsia, chronic, 574.
of Leube, 574.
without stomach lesions, 576.
gastro-intestinal, chronic, 624.
intestinal, dependant upon fermentation, 624.
motor, due to hypermotility, 617.
due to hypomotility, 617.
nervous, due to neurasthenia, 615.
due to organic diseases, 615.
sensory, appetite in, 616.
gastralgia in, 616.
mental condition in, 616.
psychic influences in, 616.
symptoms of, due to organic constriction at pylorus, 579.
Dysphagia, 870.
Dyspituitarism, 1158.
Dyspnea, in nephritis, 807.
in pleurisy, 391.
influence of, on endocarditis, 489.
with uremia, 765.
Dystrophia adiposo-genitalis, 1159.
Dystrophy, muscular. See Muscular Dystrophy.

E

Ear, affection of, by influenza, 128.
effect on, of scarlet fever, 329.
of congenital syphilis, 66.
involvement of, in typhoid, 113.
paralysis of auditory nerve, 868.
Echinococcus. See Cestodes.
Eclampsia, mortality from, 795.
symptoms in prognosis of, 795-796.
Eclampsia infantum. See Infantile convulsions.
Ectasia, 726.
Eczema, associated with bronchial asthma, 369.
Edema, acute circumscribed. See Angioneurotic edema.
in chronic nephritis, 802.
of extremities, in cancer of liver, 709.
of glottis, in syphilis, 33.
of larynx, 362.
of leg, persistent hereditary, 1080.
of pharynx, 559.
Edema, pulmonary, 375.
Ehrlich, therapy of, 35.
Electrical chorea, 1046.
Elephantiasis, due to filariasis, 316.
Elephantiasis neuromatosa, 884.
Elephantoid fever, due to filariasis, 316.
Emaciation, in brain tumor, 995.
in diabetes mellitus, 1114.
Embolic infarcts, in diphtheria, 140.
Embolism, cerebral, 953.
of hepatic artery, 680.
spinal, 929.
Emphysema, pulmonary, associated conditions of, 383-384.
atrophic, 385.
compensatory, 382.
fixed thorax in, 383.
heredity considered in, 383.
hypertrophic, 383.
occupations in, 383.
surgical, 382.
sex considered in, 383.
Empyema, 392.
and pneumonia, 164, 165, 393.
double, 394.
general statements on, 393.
lung abscess with, 393.
parapneumonic, 394.
prognosis of, during early life, 394.
time of complication in, 394.
with metastases, 393.
with rheumatism, 288.
Empyema necessitatis, 394.
Encephalitis, acute, 974.
following arsenical poisoning, 976.
of children, 977.
aphasia with, 979.
causes of, 979.
contractures in, 979.
epilepsy in, 979.
symptoms of, 979.
causative origin of, 973.
chronic, 974.
due to arsenical poisoning, 976.
due to influenza, 129.
due to salvarsan, 976.
hemorrhagic, 974.
cure of, 974.
influenza hemorrhagic, 975.
lumbar puncture in, 975, 977.
meningo-encephalitis, 974.
paralysis with, 975.
polioencephalitis superior, 975.
polioencephalomyelitis, 976.
primary acute hemorrhagic, 976.
prognosis of, 974.
purulent. See Brain Abscess.
secondary to acute infections, 973.
suppurative. See Brain Abscess.
traumatic, 974.
with small brain abscesses, 974.
Encephalopathy, in lead multiple neuritis, 851.
lead, 1189.
Endarteritis, specific, cerebral thrombosis with, 956.

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Endarteritis, specific, in cerebral syphilis, 42-43.
spinal, 929.
Endarteritis chronica deformans, 402.
Endarteritis chronica nodosa, 402.
Endocarditis, acute septic, avenues of entrance of infecting agent, 472.
benign and malignant types of, 473.
cerebral form of, 476.
chronic cardiac, 476.
fulminating intermittent type of, 475.
intermittent or pyemic form of, 474-475.
involvement by, 473-474.
origin of, 472.
preceding valvular disease, 472.
process of, 471-472.
typhoid form of, 476.
acute simple, 469.
bacterial invasion of, 469.
complications of, 470.
duration of, 471.
extent of damage done by, 469.
involvement of, 469.
physical signs of, 470-471.
prominent lesion of, 469.
relapses of, 470.
and pneumonia, 167, 485.
arteriosclerotic, 504.
cerebral hemorrhage due to, 960-961.
chronic, age in, 484.
anatomic cure of valvular lesions in, 493.
blood condition in, 491.
decompensation in, 482.
degenerative process of, 478.
dilatation in, 480.
blood pressure in, 481.
conditions of, 481.
hypertrophy of left ventricle, 481.
of left ventricle, 481.
with aortic insufficiency, 481.
dropsies in, 492.
duration of, 494-495.
frequency of valvular lesions in, 483.
heredity and family history in, 483.
inflammatory process of, 478.
influence of treatment on prognosis of, 493.
influence on, of cardiac asthma and dyspnea, 489.
of erysipelas, 486.
of induration of lung, 490.
of infections, 485.
of intercurrent diseases, 486.
of marriage and pregnancy, 486-487.
of pericarditis, 489.
of pneumonia, 485.
of respiratory diseases, 489.
of tuberculosis. See Cardiovascular Tuberculosis.
nature of, 477.
nephritis with, 491.
nervous system in, 492.
occupation and social conditions in, 484.
prognosis of, 478.
Endocarditis, chronic, prognosis of, compensatory hypertrophy, 479-480.
reserve force of heart, 479.
prognostic significance of physical signs, 494.
psychic element in, 492-493.
pulse in, 492.
reaction of, to digitalis, 494.
sex in, 483.
skin condition in, 491.
sudden death from, 493.
valvular anomalies in, 493.
with hypertrophy, 478.
x-ray examination in, 492.
due to arthritis, 283.
gonococcus, 132, 190, 476.
in chorea, 1042.
in typhoid fever, 96.
infections in, 471, 485.
liver complications with, 491.
malignant, 131, 284, 471, 486.
mild, in children, with chorea and rheumatism, 284.
non-septic malignant rheumatic, 473.
origin of, 468.
pathology of, 468.
scarlatinal, 330.
severe, in children, with chorea and rheumatism, 284.
syphilitic, 504.
tuberculous, 275.
ulcerative, 471.
varieties of, 468.
with cholelithiasis, 731.
with diphtheria, 140.
Endocarditis verrucosa, 469.
Endothelioma, 999.
primary, 1171.
Enteric fever. See Typhoid Fever.
Enteritis, acute, cholera morbus, 623.
acute catarrhal, 619.
constipation with, 620.
diarrhea with, 620.
due to ptomaine poisoning, 620.
primary, 620.
prognosis of, 620.
recovery from, 620.
secondary, 620.
acute croupous, 621.
acute diphtheritic, 621.
acute membranous, 622.
infantile, 623.
infections in, 622.
nervous or hysterical, 622.
acute phlegmonous, 621.
acute ulcerative, 621.
constriction due to, 621.
alcoholic, 1181.
chronic, causes of, 623, 625.
due to opium, 625.
gastrogenic diarrhea, 624.
intestinal dyspepsia dependent upon fermentation in, 624.
of nervous origin, 625.
of warm countries, 626.

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Enteritis, chronic, sprue, 626.
croupous, 621.
secondary chronic, primary causes of, 625.
tuberculous, 253.
ulcerative tuberculous, 233.
Enteropathia dyspeptica chronica, 624.
Entozoa, of brain, 997.
Eosinophilia, in chorea, 1041.
Ephemeral fever, 350.
Epidemic cerebrospinal meningitis, 177.
Epilepsy, abortion of seizures in, 1052.
amblyopia in, 1051.
amnesia in, 1053.
and pregnancy, 1051.
and vertigo, 870.
aura in, 1052.
Babinski phenomenon in, 1052.
complications in, 1052.
convulsions of, 1047.
course of, 1052.
definition of, 1046.
delirium of, 1053.
dementia in, 1053.
due to acute infections, 1051.
due to alcoholism, 1050.
due to cortical irritation, 1047-1048.
due to dietetic errors, 1051.
due to fright, 1051.
due to sunstroke, 1051.
due to syphilis, 1050.
due to traumatism, 1050.
essential or idiopathic, surgery for, 1058.
focal. See Secondary Epilepsy.
jacksonian, 1047.
following cerebral palsies of childhood, influence of heredity on production of, 977.
grand mal, 1046.
dislocation of humerus in, 1053.
postepileptic period, 1054.
recurrence of, 1054.
in encephalitis, acute, of children, 979.
insanity in, 1053.
jacksonian, 1055.
loss of self-control in, 1053.
mania, with homicidal tendencies in, 1053.
mental lethargy in, 1053.
merging of forms of, 1047.
migraine with, 1062.
nocturnal, 1054.
ocular anomalies in, 1051.
pathogenesis of, 1048.
petit mal, 1046, 1055.
postepileptic period in, 1054.
posthemiplegic, 1050.
primary, 1047.
age in, 1048.
due to alcoholism, 1050.
due to syphilis, 1050.
due to traumatism, 1050.
family, 1049.
heredity in, 1049.
prognostic factors in, 1048.
sex in, 1050.
Epilepsy, prognostic factors in, diet, 1051.
disordered nutrition, 1052.
psychic, 1046, 1055.
secondary, 1055.
blood condition in, 1056.
bromid treatment for, 1057.
complicated by meningitis or meningo-encephalitis, 1055.
complications in, 1056.
course of, 1056.
cure of, 1057.
danger of death in attacks of, 1056.
general condition of patient in, 1057.
manner of death in, 1056.
operation for, 1055.
pneumonia with, 1056.
pulmonary edema with, 1056.
pulmonary tuberculosis with, 1056.
remissions and relapses in, 1057.
with organic nervous disease, 1056.
senile, 1049.
status epilepticus in, 1054.
syphilitic, 42, 1050.
with hydrocephalus, 945.
Epileptic convulsions, in lead encephalopathy, 1190.
Epileptic equivalent, migraine with, 1062.
Epileptic equivalents, 1046, 1055.
in brain tumor, 994.
Epileptiform seizures, 1047.
hysterical, 1014.
in multiple sclerosis of brain and cord, 910.
in tabes dorsalis, 59.
Epinephritis, 835.
Epistaxis, causes of, 359.
in children, 360.
in chronic interstitial nephritis, 809.
in cirrhosis, 690.
in typhoid fever, 97.
Epithelial casts, 750.
Erb's paralysis, 876.
Erb's syphilitic spinal paralysis, 37.
Erysipelas, albuminuria in, 176.
and endocarditis, 486.
blood condition in, 176.
circulatory disturbances in, 175.
complications influencing growth of, 174.
conclusions on, 176.
etiology of, 173.
in alcoholics, 174.
in typhoid fever, 107.
manifestations of, general, 175-176.
local, 174.
meningitis, purulent, with, 176.
of aged, 174.
of newborn, 174.
parotitis, metastatic, with, 176.
period of incubation of, 174.
port of entry of, 173.
puerperal, 174.
respiratory system in, 176.
streptococcus erysipelatis of, 173.
with chronic disease, 174.

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Erythema multiforme, alternation of chronic purpura with, 546.
Erythema nodosum, 289.
resemblance to, of purpura rheumatica, 544.
Erythremia, primary, associated conditions of, 550.
blood picture of, 550.
nature of, 549.
symptoms of, 549.
secondary, leading primary diseases of, 551.
prognosis of, 551.
Erythromelalgia, 415.
and Raynaud's disease, 1067.
associated symptoms of, 1067, 1068.
characteristic symptoms of, 1066.
chronic, 1068.
course of, 1068.
definition of, 1066.
destructive processes in, 1067.
duration of, 1068.
morphinism due to, 1069.
pathological findings of, 1066.
prognosis for life in, 1069.
Esophageal stricture, benign, 566.
congenital, 567.
extra-esophageal, 566.
malignant, 566.
symptoms of, 567.
Esophagismus, 565.
hysterical, 1014.
Esophagitis, acute, 562.
catarrhal, acute, 562.
chronic, 563.
corrosive, 564.
croupous, 564.
diphtheritic, 564.
phlegmonous, 563.
pustular, 563.
ulcerative, 564.
Esophagus, cancer of, 566.
dilatation of, 568.
diverticula of, pressure or pulsation, 569.
traction, 569.
diseases of, cancer, 567.
dilatation, 568.
diverticula, 569.
rupture, 568.
spasm and paralysis of, 565.
fibrous thickening of, 568.
inflammatory or ulcerative changes of, 562.
lipomata of, 568.
neoplasms of, 567.
paralysis of, 565.
polypi of, 568.
rupture of, 568.
spasm of, 565.
syphilis of, 34.
tuberculosis of, 253.
varices of, 565.
Estivo-autumnal fever. See Malaria.
Exophthalmic goiter, atypical, 1148.
relapse in, 1150.
Exophthalmic goiter, clinical forms of, 1140.
compression of, for treatment, 1142.
heredity in, 1141.
in tuberculosis, 242.
manipulation of, 1142.
minimum symptoms of, cardiovascular, 1139.
sympathetic, 1139.
tremor and singular ocular symptom, 1139.
mortality from, 1151.
in operated cases, 1152.
myxedema in, 1147.
ocular symptoms in, 1145.
operative treatment of, 1151.
size of swelling in, 1145.
symptoms of, 1139.
typical, relapse in, 1150.
typical acute, 1141.
development of, 1141.
gastro-intestinal symptoms in, 1141.
mental torpor in, 1141.
symptoms of, 1141.
x-ray in, 1142.
typical and atypical types of, 1140.
typical chronic, acromegaly in, 1148.
blood picture in, 1148.
blood pressure study of, 1144.
cardinal symptoms of, 1142.
cardiovascular symptoms in, 1143.
complications referable to nervous system in, 1143, 1146.
digestive disturbances in, 1146.
eye symptoms in, 1145.
genito-urinary organs in, 1147.
glucosuria and diabetes in, 1147.
leading clinical manifestations of, 1142.
loss of weight in, 1146.
mental state in, 1146.
Musset's phenomenon in, 1144.
myxedema in, 1147.
prognostic significance of leading clinical features in, 1143.
pulse amplitude in, 1144.
respiratory symptoms in, 1146.
skin changes in, 1147.
spasm in, 1144.
sweating in, 1146.
tremor in, 1144.
Extensor paralysis, in lead multiple neuritis, 851.
Extragastric bleeding, 613.
Extrasystoles, irregularities due to, 448.
Eye, affection of, in tabes dorsalis, 54, 56.
effect on, of arteriosclerosis, 415, 418.
of cerebral syphilis, 43.
of juvenile tabes, 47.
of measles, 345.
involvement of, in typhoid, 113.
lesions of, in congenital syphilis, 67.
Eye complications, in gout, 1105.

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F.

Facial hemiatrophy, causes of, 863.
nature of, 863.
Facial paralysis, 847.
causes of, 863.
character of, 863.
crossed with hemiplegia, 866.
double, 866.
due to pontine disease, associated conditions of, 864.
causes of, 864.
in children, 866.
location of, 863.
peripheral, 864.
reaction of degeneration in, 865.
right-sided, with aphasia and hemiplegia, 866.
with family neuropathic tendencies, 866.
Facial spasm, in neurasthenic and hysterical children, 866.
in women, 867.
tic habit due to, 866.
Faint spells, of cerebral anemia, 948.
Falling sickness, 1046.
Fallopian aqueduct, hemorrhage into, 865.
Fallopian tubes, tuberculosis of, 272.
Famine fever. See Typhus Fever.
Farcy. See Glanders.
Fat deposits, in adiposis dolorosa, 1078.
Fatty heart, associated conditions of, 453.
causes of, 452.
prognosis of, 453.
Fatty liver, and enlargement, with pernicious anemia, 712.
degeneration of, 712.
infiltration in, 712.
with appendicitis, 712.
with infectious diseases, 712.
Febris epidemica. See Influenza.
Febris recurrens. See Relapsing Fever.
Fecal vomiting, hysterical, 1018.
Fetal chondrodystrophy, 1131.
Fetal cretinism, 1131.
Fever, breakbone, 356.
dandy, 356.
enteric. See Typhoid Fever.
ephemeral, 350.
estivo-autumnal. See Malaria.
glandular, 353.
herpetic, 352.
hysterical, 1018.
intermittent. See Malaria.
Mediterranean, 196.
Neapolitan, 196.
relapsing, 82.
symptomatic, 350.
thermic, 1206.
typhoid, 84.
typhus. See Typhus Fever.
undulant, 196.
Fibrinous bronchitis, 373.
Fibroid degeneration, of myocardium, 443.
Fibroid phthisis, 379.
acute, 244.
chronic, interstitial pneumonia, 246.
Fibroid phthisis, chronic, non-tuberculous fibrosis with final tuberculization, 245.
tuberculosis ab initio, 244.
due to occupation, 380.
in pneumonia, 166.
Filariasis, 314-315.
Filaton-Duke's disease, 352.
Fistulae, biliary, with gall stones, 730.
bronchobiliary, with gall-stones, 730.
in cholelithiasis, 728.
urinary, with gall-stones, 730.
Fixed thorax, in emphysema, 383.
Flexner serum, for cerebrospinal meningitis, 184-185.
Flint murmur, 501.
Food poisoning, bacterial invasion of meat, contaminated sausage or pork, 1203.
contaminated veal, 1203.
symptoms of, 1203.
conclusions on, 1204.
due to fish and shell fish, 1204.
due to milk products, 1204.
endogenous, 1203.
epidemics of, 1203.
exogenous, 1203.
leukomain, 1203.
ptomain, 1203.
Foot and mouth disease, conveyance of, 349.
healing process of, 349-350.
nature of, 349.
symptoms of, 349.
Foramen ovale, perforate, 438.
with pulmonary stenosis, 436.
Friedreich's disease. See Hereditary Ataxia.
Fright, epilepsy due to, 1051.
Fungus infections, non-bacterial, 301.
Furuncles, in diabetes mellitus, 1118.
in paratyphoid, 123.

G

Gall-bladder, acute inflammation of, 715.
adhesions of, in cholelithiasis, 729.
cancer of, 717.
cholecystitis of, 715.
dilatation of, due to stone in cystic duct, 726.
dropsy of, 716, 726.
enlargement of, in acute biliary colic, 722.
gangrene of, 717.
in cholelithiasis, 728.
perforation of, 717.
in cholelithiasis, 728.
tuberculosis of, 256.
Gall-stones. See Cholelithiasis.
bronchobiliary fistulae with, 730.
cholangitis due to, 715.
chronic cholecystitis due to, 716.
Ganglionitis, acute posterior. See Herpes zoster.

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Gangrene, angiospastic. See Raynaud's disease.
diabetic, 1118.
in cholecystitis, 717.
in pharyngeal diphtheria, 137.
pulmonary, in cancer, 387.
in influenza, 127.
in pneumonia, 164.
in tuberculosis, 242.
symmetrical. See Raynaud's disease.
Gangrene of vulva, in typhoid, 110.
Garrod's modification of Rothera test, for acetone, 1115.
Gastralgia, 616.
in dyspepsia, 616.
Gastrectasia, 576.
Gastric neuroses, general considerations on, 615.
motor, due to hypermotility, 617.
due to hypomotility, 617.
psychic element in, 615, 619.
psychoses with, 615.
secretory anomalies of, 618.
hyperacidity, 618.
hypersecretion, 618.
sensory, 616.
Gastric tetany, 1167.
Gastric ulcer, acid condition in, 587.
acute and chronic, 587.
age and type most affected by, 587.
alcoholic, 1181.
and duodenal, relative frequency of, 587.
Aschoff's hemorrhagic erosions in, 586.
blood picture of grave anemia in, 596.
carcinomatous, 589.
carcinomatous degeneration in, 593.
chronicity and resistance to treatment of, 588.
complete, 590.
complications in, acidosis, 596.
carcinomatous degeneration, 593.
cicatricial distortion and stenosis, 595.
exhaustion, 596.
hemorrhage, 592.
parotitis (metastatic?), 596.
perforation, 590.
perigastric adhesions, 595.
tetany, 596.
examination of stomach contents in, 589.
frequency of complications in, 598.
hemorrhage in, large, into mucosa, 586.
occurrence of, 592.
repeated, 592.
history of, 585.
hourglass contraction in, 595.
hyperchlorhydria symptomatic of, 588.
indicanuria in, 588.
mortality from, 597-598.
paramount factors in cure of, 599.
partial, 590.
perforation of, "acute abdomen" in, 591-592.
early operation for, 591, 592, 599.
frequency of, 590.
Gastric ulcer, perforation of, importance of early diagnosis in, 591.
into pleural cavity, heart sac or lung, 591.
prognosis of, 590-591.
protective localized peritonitis in, 591.
protective processes in, 591.
recovery after operation for, 592.
symptoms of, 591-592.
periods of remissions of symptoms, without healing of, 588.
prognosis of, facts influencing, 587.
general facts for, 586.
significance of age and surgical treatment in, 597.
proliferative changes produced by, 588.
symptoms of, 585.
vomiting in, 589.
with nephroptosis, 829.
without subjective symptoms, 587.
x-ray for, 589.
Gastritis, acute, with organic diseases of stomach, 571.
recurring, 572.
acute forms of, acute catarrh, 570.
corrosive, 571.
of fungus origin, 572.
infectious, 570.
membranous, 571.
phlegmonous, 570.
suppurative, 572.
toxic, 571.
alcoholic, 575, 1181.
chronic, associated with or secondary to cirrhosis, 573.
blood picture in, 575.
complications of, 576.
examination of stomach contents in, 574-575.
mucosa in, 575.
nervous symptoms of, 575.
secondary to cirrhosis of liver, 573.
symptoms of, 574.
chronic forms of, cirrhotic, 572.
interstitial, 573.
mixed, 573.
parenchymatous, 573.
influenzal type of, 570.
occult blood in stool in, 588.
primary, 573.
secondary, 573.
severe, 576.
Gastritis acida, 573.
Gastroduodenitis, 620.
Gastroduodenocholangitis, 665.
Gastro-enteritis, in measles, 345.
Gastrogenic diarrhea, 624.
Gastro-intestinal diarrhea, 624.
Gastro-intestinal influenza, 128.
Gastro-intestinal symptoms, in alcoholism, 1181.
in neurasthenia, 1031.
of pellagra, 1200.
Gastro-intestinal pernicious malaria, 75.

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Gastro-intestinal tetany, 1167.
Gastroptosis, absence of tenth costal cartilage in, 580.
associated conditions in, 580-581.
causes of, 580.
Dietl's crises in, 580.
mobile kidney in, 580.
nature of, 579.
predisposition to, 579.
prognosis of, 581.
symptoms of, 580.
Gastrorrhagia, 613.
primary causes of, 614.
Gastrostasis, 615.
Gastrosuccorrhea, suggestive of ulcer, 589.
Gaucher's disease, 1171.
Genital atrophy, in infantilism, 1159.
Genital tuberculosis, in females, blood condition of, 271.
menstrual irregularities in, 271.
of fallopian tubes, 272.
ovarian, 272.
primary, 272.
uterine, 273.
vaginal, 273.
Genito-urinary system, in alcoholism, 1182.
in exophthalmic goiter, 1147.
in typhoid fever, 107.
Genito-urinary tuberculosis, 267.
blood pressure in, 270.
factors in prognosis of, 267.
persistent fever with, 270.
pregnancy and childbirth with, 270.
German measles, complications in, 346.
nature of, 346.
Gibson's rule, on blood pressure in pneumonia, 148.
Gingivitis, ulcerative, in scorbutus, 1133.
Glanders, acute, 212-213.
chronic, 213.
infection of, 212.
prophylactic methods against, 213.
Glandular fever, 353-354.
Glénard's disease, 579.
Glioma, 924-925.
of brain, 997.
Gliomatosis, spinal, 925.
Gliosis of spinal cord. See Syringomyelia.
pseudotabetic, 917.
Glomerulonephritis, chronic, 797.
Glossitis, with pernicious anemia, 528.
Glossopharyngeal paralysis, 870.
Glottis, edema of, 362.
in syphilis, 33.
stenosis of, in syphilis, 33.
Glucosuria, in alcoholics with polyneuritis, 1118.
alimentary, following anesthesia, 1110.
following drinking of beer, etc., 1110.
functional origin of, 1109.
relation of, to diabetes, 1109.
tolerance to sugar assimilation, 1108.
Glucosuria and diabetes, in exophthalmic goiter, 1147.
due to adrenalin, 1107.
due to anesthesia, 1110.
due to hypophysis disease, 1107.
due to liver disease, 1107.
due to skeletal muscles, proteid and fat, 1108.
due to surgical lesions, 1119.
due to thyroid extract, 1107.
due to traumatism, 1108.
in diabètes bronzé, 1107.
in diabetes mellitus, 1106.
in pancreatic disease, 1106.
negative factors in, contagion, 1108.
kidney, 1108.
phloridzin, 1108.
Gluteal nerves, paralysis of, 881.
Goiter, acromegaly and, 1161.
and hyperthyroidea, 1149.
association of, 1137.
with soil and water, 1138.
complications in, 1138.
distribution of, 1137.
endemic, 1137.
endemic areas in, 1137.
exophthalmic. See Exophthalmic goiter.
frequency of, 1137.
heredity in, 1137.
infections in, 1138.
influencing factors in, 1137.
return of, 1138.
spontaneous recovery from, 1138.
with lymphatic and nervous temperament, 1138.
Goiter heart, 1139-1149.
Gonococcus arthritis, 192.
Gonococcus endocarditis, 132, 190, 476.
blood condition in, 191.
clinical manifestations of, 190.
complications in, 191-192.
types of, intermittent or pyemic, 190.
irregular, 191.
typhoid, 190.
Gonococcus infection, 132.
gonococcemia, 189.
gonococcus arthritis, 192.
gonococcus endocarditis, 190.
Gonorrhea, myelitis secondary to, 906.
multiple neuritis, 855.
rheumatism, 192.
Gout, abarticular, 1103.
acute, course of, 1102.
determining symptoms of, 1102.
duration of, 1102.
evidences of approaching remission in, 1102.
initial symptoms of, 1101.
monarthritic cases of, 1102.
causative factors of, age, 1100.
diet, 1101.
habits, 1100.
heredity, 1100.
lead poisoning, 1101.
lowered standard of health, 1101.

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Gout, causative factors of, sex, 1100.
chemical conclusions in, 1099.
chronic, extent of joint changes in, 1103.
limitation of, to joints, 1103.
ulcerative articular processes in, 1103.
chronic articular, 1103.
complications in, cardiac, 1104.
dyspepsia, 1104.
gastro-intestinal, 1104.
kidney, 1104-1105.
liver, 1105.
of eye, 1105.
of nervous system, 1104.
pulmonary, 1105.
skin lesions, 1104.
definition of, 1099.
diabetes mellitus and, 1119.
history of, 1099.
in cirrhosis, 695.
irregular, 1103.
complications in, 1104.
theories on, Brugsch, 1099.
Epstein, 1098.
Garrod, 1098.
Haig, 1098.
Klemperer, 1098.
Kolisch, 1098.
Luff, 1099.
Mordhorst, 1098.
von Noorden, 1098.
Roberts, Sir William, 1098.
Schittenhelm, 1099.
uric acid phenomenon in, 1099.
Gouty conditions, in tuberculosis, 242.
Grand mal, 1046.
humerus in, 1053.
Granular casts, 749-750.
Granuloma, syphilitic, 541.
Graves' disease, 249, 1142.
Green sickness, 517.
Grippe. See Influenza.

H

Habit paralysis, 847.
Hay fever, blood picture of, 358.
nature of, 358.
surgical treatment for, 359.
use of cocaine for, 359.
vaccination against, 359.
Headache, bilious. See Migraine.
blind. See Migraine.
hysterical involvement of, 1011.
in brain tumor, 992.
sick. See Migraine.
Heart, aneurism of, 467.
congenital defects of, defective interventricular septum, 438.
dextrocardia, 438.
insufficiency and stenosis of mitral and tricuspid valves, 439.
perforate and premature closure of ductus arteriosus, 439.
perforate foramen ovale, 438.
stenosis of aortic orifice, 438.
Heart, congenital defects of, stenosis of pulmonary orifice, 435.
transposition of aorta and pulmonary arteries, 439.
delirious, 510.
fatty, 452.
functional disorders of, bradycardia, 511.
causes of, 506-507.
neurasthenic state, 512.
palpitation, 507.
tachycardia, simple, 510.
hypertrophy and dilatation of, 460.
hypertrophy of, idiopathic, 441.
inherent muscular weakness of, 465.
irritable, 510.
palpitation of, 507.
parasites of, 466.
senile, 460.
syphilis of, 28.
Heart anomalies, in chorea, 1042.
Heart block. See Stokes-Adams disease.
Heart changes, degenerative, in alcoholism, 1182.
in chronic interstitial nephritis, 806-807.
in gout, 1104.
in measles, 345.
Heart condition, in appendicitis, 653.
in cirrhosis, 687.
in leukocytic leukemia, 532.
in pernicious anemia, 526.
Heart disease, hemoptysis of, 376.
causing congested kidney, 812.
Heart weakness, due to insufficient exercise, 464.
Heatstroke. See Sunstroke.
Heberden's nodes, in arthritis deformans, 1091.
Heine-Medin disease. See Poliomyelitis, 317.
Hemachromatosis, with pigmented cirrhosis, 696.
Hematemesis, hysterical, 614.
in cancer of stomach, 604.
in cirrhosis, 689.
primary causes of, 613-614.
Hematoma, spinal, 931.
Hematomyelia, 930.
spontaneous, 930.
Hematorrhachis, 930.
Hematuria, conditions indicated by, 755.
acute and chronic primary infections, 759.
constitutional diseases, 760.
echinococcus disease. See Cestodes.
hemorrhagic, with infections, 760.
nephritis, tuberculous, 759.
acute tubal, 756.
chronic interstitial, 756.
chronic tubal, 756.
new growth of kidney, 760.
paroxysmal hematuria following chilling of surface, 758.
pyelitis, non-calculous, 759.
renal epistaxis, 757.

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Hematuria, conditions indicated by, renal hematuria with gouty diathesis, 758.
renal infarct, with septic fever, 758.
rupture of kidney, 760.
stone in kidney, 759.
cystoscopic examination in, 753.
effects of, 754.
essential, 757.
in cirrhosis, 690.
origin of, 753.
paroxysmal, following chilling of surface, 758.
with chronic nephritis, 801.
renal, 754.
with gouty diathesis, 758.
Hemianesthesia, hysterical, 1009-1010.
in cerebral hemorrhage, 969.
Hemianopia, bilateral vertical, 858.
binasal, 859.
bitemporal, 858.
blindness due to, 859.
double, 858.
functional, with migraine or hysteria, 859.
in cerebral hemorrhage, 970.
lateral or homonymous, 859.
one-sided, 858.
temporal, 858.
Hemiataxia, in cerebellar disease, 1004.
Hemiatrophy, facial, 863.
Hemicrania. See Migraine.
Hemicrania sympatheticotonica, 1062.
Hemicrania sympatheticoparalytica, 1062.
Hemihypotonia in cerebellar disease, 1004.
Hemiplegia, cerebral hemorrhage supposed cause of, 958.
due to cerebral embolism and diphtheria, 954.
in brain tumor, 991.
in cerebral hemorrhage, 969.
in cerebral syphilis, 43.
in diphtheria, 954.
in diphtheritic paralysis, 141.
in syphilis, 43.
spastic infantile, 977.
with aphasia and facial paralysis, 866.
Hemocytozoa, 72.
Hemoglobinuria, paroxysmal, 761.
periodic, 761.
toxic, 761.
Hemopericardium, 433.
Hemophilia, 548.
hemoptysis of, 377.
Hemoptysis, in cirrhosis, 690.
of bronchitis, 377.
of heart disease, 376.
of hemophilia, 377.
of hyperemia, 376.
Hemorrhage, anemia due to, 514.
cerebellar, 1003.
cerebral, 957.
danger point in, 515.
extragastric, 614.
in cholelithiasis, 731.
in gastric ulcer, 586-592.
Hemorrhage, into spinal membranes and cord. See Spinal hemorrhage.
intragastric, 614.
pulmonary. See Pulmonary Hemorrhage.
regeneration from, 515-516.
retinal, with pernicious anemia, 527.
Hemorrhagic diathesis. See Purpura.
Hemorrhagic pancreatitis, 737.
Hemorrhagic pleurisy, 396.
Hemorrhagic symptoms, of pharynx, 559.
Hemosporidia, 72.
Henoch's purpura, 547.
Hepatic and intra-hepatic ducts, obstruction of, 726.
Hepatic artery, diseases of, aneurism, 680.
arteriosclerosis, 680.
embolism, 680.
enlargement, 681.
thrombosis, 680.
Hepatic calculi. See Cholelithiasis.
Hepatic vein, diseases of, complete occlusion, 679.
thrombosis, 679.
Hepatitis, suppurative, 704.
Hereditary ataxia, complications in, 888.
course of, 887.
Marie's, 888.
nature of, 887.
symptoms of, 887.
Hernia, hiccough with, 875.
Herpes labialis, in pneumonia, 161.
Herpes zoster, accompanying symptoms of, 886.
classification of, 885.
confluence in, 886.
course of, 886.
definition of, 885.
duration of, 886.
epidemics of, 885.
hemorrhagic form of, 886.
malignant, 886.
sacral, 886.
vesicles and inflamed base of, 885.
Herpetic fever, 352.
Herxheimer reaction, in edema of glottis, 33.
Hiccough, causes of, 875.
easily controlled, 875.
hysterical, 875.
in appendicitis, 653.
indicative of virulent infection, 875.
with deep coma, 875.
with hemorrhagic pancreatitis, 875.
with hernia, 875.
with inflammatory disease, 875.
with peritonitis, 875.
with toxemia, 875.
with typhoid fever, 875.
Hippocrates, aphorisms of, 2.
genuine treatises of, 3.
rules of practice of, 2.
Hirschsprung's disease, 632, 640.
Hodgkin's disease, acute, 538.
latent type of, 539.

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Hodgkin's disease, acute, non-relapsing, 538.
Pel and Ebstein's process of, 538.
relapsing, 538.
chronic, blood picture in, 539.
bronzing of skin in, 539.
duration of, 540.
hemorrhagic symptoms of, 541.
mediastinal glands in, 539.
période cachectique of, 540.
période latente of, 540.
période progressive of, 540.
remissions in, 540.
definition of, 536.
diphtheroid organism in, 537.
distinguished from tuberculous lymphadenitis, 266.
leading causes of death from, 541.
pathologic changes in lymph glands in, 537.
resemblance of, to tuberculosis, 537.
surgical treatment of, 541.
symptom-complex of granuloma, 538.
symptom-complex of lymphocytoma, 537.
Hookworm. See Ankylostomiasis.
Hourglass stomach, in gastric ulcer, 595.
Huntington's chorea, 1044.
Hutchinsonian teeth, 67.
Hyaline casts, 749, 751.
Hydatid disease, cause of, 306.
cysts of, 306.
of brain, 308.
of kidney, 308.
of liver, death due to, 308.
latent, 307.
perforation in, 307.
suppuration, 307.
of lung, 308.
of other organs, 309.
of spleen, 308.
Hydrocephalus, acquired, acute exacerbations with, 943.
chronic, 943.
simulating brain tumor, 943.
symptoms of, 943.
congenital, 67.
appearance of, 944.
arrested, 944.
causes of, 944.
complications in, 945.
death due to intercurrent disease in, 945.
duration of, 944.
effect of, on intelligence, 945.
family type of, 944.
menstrual anomalies in, 945.
moderate, 945.
spinal fluid in, 945.
spontaneous rupture of, 944.
syphilitic, 944-945.
due to epidemic cerebrospinal meningitis, 182.
epilepsy with, 945.
idiopathic internal, 943.
Hydromyelus, 914.
Hydronephrosis, acquired, 816, 817.
Hydronephrosis, acute infection with, 818.
advanced, prognosis of, 819.
anuria in, 817.
bilateral, 817.
causes of, 815.
cause of death in, 817.
chronic, 818.
complications in, 818.
congenital, causes of, 816.
operation for, 819.
prognosis of, 818.
definition of, 815.
early recognition of, 818.
general condition of patient in, 818.
intermittent, 820.
nephrectomy for, 819.
prognostic conclusions on, 819.
prognostic factors in, 816.
purulent, 818.
rupture of, 818.
secondary bladder and ureteral changes in, 820.
unilateral, condition of second kidney in, 818.
prognosis of, 819.
uremia due to, 818.
with nephroptosis, 829.
Hydropericardium, 274, 433.
Hydrophobia, nature of, 354.
Pasteur treatment of, 355.
period of incubation of, 354-355.
prognosis of, 355.
stages of, 355.
statistics on, 356.
symptoms of, 355.
Hydropneumothorax, 396.
Hydrops articulorum, 1079.
Hydrops articulorum intermittens, 1079.
Hydrothorax, 396.
associated symptoms of, 396.
causes of, 396.
Hyperacidity, 618.
Hyperchlorhydria, 618.
Hyperemia, hemoptysis of, 376.
of brain. See Cerebral Hyperemia.
of kidney, 811.
of liver, active, 676.
passive, 676.
of pharynx, 559.
of spinal cord, 928.
Hyperesthesia, 616.
Hyperesthetic areas of Head, 840.
Hypermotility, belching of gas in, 617.
nervous vomiting in, 617.
peristaltic unrest of Kussmaul in, 617.
pylorospasm in, 617.
rumination in, 617.
Hypernephroma, 826.
Hyperosmia, 857.
Hyperostoses, diffuse, 1094.
of skull, 1095.
Hyperpeptica, 573.
Hyperpituitarism, 1160.
Hyperpyrexia, in acute biliary colic, 721.
in sunstroke, 1205.
with arthritis, 286.

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Hypersecretion, 618.
Hypertension, compensatory, in chronic nephritis, 802.
in chronic interstitial nephritis, 806-807-808.
Hyperthyroidea, atypical, 1148-1149.
clinical features of anomalous types of, 1140.
chronic typical, 1142.
due to degeneration of innocent small or large chronic goiters, 1140.
exophthalmic goiter, 1139.
goiter and, 1149.
in children, 1151.
mortality from, 1151.
in operated cases, 1152.
myxedema-cretinism, 1153.
protean character of, 1140.
psychic element in, 1151.
self-limitation of, 1150.
spontaneous cure of, 1150.
symptoms of, without goiter, 1139.
thymus enlargement in, 1145.
thyroid neoplasm in, 1150.
Hypertrophic muscular dystrophy, 896.
Hypertrophy, and dilatation of heart, due to hypertension, 461.
due to overstrain, 460.
compensatory, in chronic nephritis, 802.
of heart, due to masturbation, 462.
due to uterine fibroids, 462.
idiopathic, 441.
secondary to other conditions, 462.
of left ventricle, in chronic interstitial nephritis, 806.
Hypnosis, for hysteria, 1009.
Hypochlorhydria, 618.
Hypochondriasis, sexual, 1028.
Hypoglossal paralysis, causes of, 873-874.
symptoms of, 873.
Hypomotility, 617.
pyloric insufficiency with, 617.
Hypoparathyroidism, 1035.
Hypophysis, disease of, glucosuria due to, 1107.
Hypopituitarism, 1158.
Hypostatic congestion, in typhoid fever, 98.
Hypotonia, in tabes dorsalis, 56.
Hysteria, acquired predisposition to, 1007.
akinesia algera in, 1017.
amnesia in, 1009.
anomalous mental states of, 1015.
appetite in, perverted, 1017.
associated with organic disease, 1019.
atasia-abasia in, 1016.
bradycardia of, 1019.
cataleptic conditions in, 1016.
"cathartic method" of Freud for, 1008.
constipation of, 1017.
contractures of, 1014.
contradictory nature of symptoms of, 1009.
cough of, 1018.
death never due to, 1020.
diarrhea of, 1017.
Hysteria, duration of psychoses in, 1009.
element of suggestion in, 1007.
emotional element in, 1009.
favorable influence of change on, 1020.
fecal vomiting of, 1018.
fever of, 1018.
forecast of behavior of individual symptoms in, 1007, 1008.
general prognosis of, 1020.
"grande hysterie" of Charcot, 1016.
hearing, involvement of, 1011.
hypnosis for, 1009.
hypnotic conditions of, 1016.
improvement of social status in, 1015.
in tabes dorsalis, 59.
influence of etiology on control of symptoms in, 1006.
inherited predisposition to, 1007.
internal organs in, 1017.
joint manifestations of, 1015.
latency of symptoms in, 1008.
loss of muscular sense in, 1016.
membranous colitis of, 1018.
Ménière symptoms in, 869.
menstrual anomalies of, 1018.
mimicry of cancer by, 1017.
monoparalysis of, 1013.
mutability of symptoms in, 1006.
ocular anomalies of, amblyopia, 1012.
asthenopia, 1012.
blindness, 1012.
contractures of ocular muscles, 1013.
contraction of visual field, 1011.
errors of accommodation, 1012.
faulty color perception, 1012.
palpebral and bulbar, 1013.
paralysis of eyelids, 1013.
paralysis of ocular muscles, 1013.
pupillary phenomenon, 1013.
organic disease following, 1020.
pains of, simulating organic disease, 1010.
paralysis of, 1013.
of vocal cords, 1014.
previous history in, 1007.
psychic disturbances or events in, 1007.
psychical nature of, 1005-1006.
psychic-sexual factors in, 1007-1008.
psychopathic and neuropathic condition in, 1006.
recurring autosuggestion in, 1005.
reflex excitability in, 1015.
secretory dsturbances of, 1018.
sensory disturbances due to anesthesia, 1009-1010.
hemianesthesia, 1009-1010.
pain, 1010.
special senses, 1011.
various, 1009.
sexual anomalies of, 1018.
simulating organic diseases, 1005, 1019.
smell, perversion of, 1011.
spasms of, epileptic, 1014.
esophagismus, 1014.
various forms of, 1014.
special senses in, hearing, 1011.

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Hysteria, special senses in, sight, 1011.
smell, 1011.
taste, 1011.
stigmata of Charcot in, 1005.
sudden cessation of symptoms in, 1007-1008.
tachycardia of, 1019.
taste, perversion of, 1011.
torticollis in, 1019.
traumatic. See Traumatic Neurosis, 1021.
trophoneuroses of, 1018.
vasomotor disturbances of, 1018.
vomiting of, 1017.
Hysterical temperament, 1015.
grave mental disease with, 1016.
social status in, 1015.
Hystero-epilepsy, 1014.

I

Icterus, 664.
Icterus gravis, 674.
Icterus neonatorum, grave familial, 671.
infections, 671.
mortality from, 672.
obstructive, due to organic lesions in duct or liver, 671.
physiologic, 670.
Idiocy, amaurotic family, cause and pathology of, 903.
symptoms of, 903.
Idiopathic hypertrophy of heart, 441.
Indian Kala-azar, 83.
Indicanuria, and constipation, 781.
associated with gastro-intestinal indigestion, 780.
auto-intoxication, 780.
bacterial action in, 782.
conditions indicated by, 781.
due to lesions of intestinal mucosa, 781.
in appendicitis, 654.
in duodenal ulcer, 588.
process of, 780.
prognostic significance of, 780.
Infantile convulsions, causes of, 1065.
cerebral hemorrhage due to, 960.
influence of, on acute infections, 1065.
predisposition to, 1065.
serious nature of, 1066.
symptomatic nature of, 1065.
Infantile Kala-azar, 83.
Infantile paralysis. See Poliomyelitis, 317.
Infantilism, adiposity in, 1159.
ateliosis in, 1159.
cause of, 1158.
cretinoid, 1159.
general, 1159.
general adiposity and undeveloped genitals in, 1159.
genital atrophy in, 1159.
of Fröhlich type, 1159.
partial, 1159.
prognosis of, 1160.
progeria in, 1159.
types of, 1159.
Infections, acute, congested kidney due to, 811.
tetany associated with, 1167.
acute and chronic primary, hematuria due to, 759.
influence of, on endocarditis, 485.
neuralgia due to, 839.
Infectious diseases, specific, bacterial, anthrax, 209.
Asiatic cholera, 197.
bacillary dysentery, 193.
diphtheria, 134.
epidemic cerebrospinal meningitis, 177.
erysipelas, 173.
glanders, 212.
gonococcus infections, 189.
influenza, 124.
leprosy, 214.
malta fever, 196.
metastatic parotitis, 300.
paratyphoid disease, 121.
plague, 201.
pneumococcus infection, 145.
pyogenic infections, 130.
rheumatic fever, 278.
tetanus, 206.
tonsillitis, 292.
tuberculosis, 216.
typhoid fever, 84.
typhus fever, 117.
of doubtful or unknown origin, dengue, 356.
ephemeral fever, 350.
foot and mouth disease, 349.
fourth disease, 352.
German measles, 346.
glandular fever, Pfeiffer's disease, 353.
herpetic fever, 352.
hydrophobia, 354.
infectious jaundice, 350.
measles, 342.
parotitis, epidemic, 352.
poliomyelitis, 317.
scarlet fever, 327.
smallpox, 333.
sweating sickness, 351.
varicella, 341.
yellow fever, 347.
due to metazoan parasites, cestodes, 303-304.
nematodes, 309.
trematodes, 316.
non-bacterial fungus, actinomycosis, 301.
protozoan, amebic dysentery, 78.
Leishmaniasis, 83.
malaria, 72.
relapsing fever, 82.
syphilis, 15.
trypanosomiasis, 81.
Infectious jaundice, 350.
Inflammatory rheumatism. See Rheumatic Fever.
Influenza, and neurasthenia, 1027.
bacteriology of, 125.

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Influenza, catarrhal, 125.
albuminuria with, 125-126.
bronchiectasis with, 127.
bronchitis with, 127.
complications in, 125-126.
ear complications in, 128.
enlarged spleen of, 125.
gangrene of lung with, 127.
pleurisy with, 127.
pneumonia with, 126.
pulse and heart changes with, 127.
tuberculosis with, 127.
character of, 124.
epidemics of, 124.
gastro-intestinal, 128.
mortality from, 125.
of nervous system, complications due to organic change in, 129.
primary invasion by, 129.
respiratory, 125.
Influenzal brain abscess, 129.
Influenzal fever, 130.
Influenzal meningitis, pneumonia with, 126-127.
Influenzal pneumonia, 126-127.
chill with, 151.
migratory type of, 126.
Infraclavicular paralysis, 877.
Insanity, due to psychasthenic states, 1030.
in epilepsy, 1053.
Insolation. See Sunstroke.
Intercostal neuralgia, 842.
Intermittent claudication, 414.
Intermittent fever. See Malaria.
Interventricular septum, 438.
Intestinal changes, in alcoholism, 1181.
Intestinal dyspepsia, dependent upon fermentation, 624.
Intestinal hemorrhage, in amebic dysentery, 80.
in paratyphoid, 123.
in typhoid fever, 102, 103, 104.
Intestinal obstruction, complete acute, 635.
complete, causes of, 634-635.
extra intestinal pressure, 639.
fecal accumulations, 639.
intussusception, 637.
strangulation, 636.
stricture, 638.
tumors or foreign bodies in bowels, 638.
volvulus, 637.
of large intestine, 634.
of small intestine, 634.
symptoms of, 635.
due to appendicitis, 656.
in cholelithiasis, 729, 731.
nature of, 633.
partial, causes of, 633-634.
chronic adynamic, 634.
symptoms of, 633.
Intestinal parasites, in beriberi, 1201.
Intestinal stricture, due to carcinoma, 638.
Intestinal stricture, due to cicatrization, 638.
due to congenital defects, 638.
due to multiple ulcers, 621.
Intestinal toxemia, chronic, 781.
Intestinal tuberculosis, 253.
primary, 253.
secondary, 254.
Intestines, affection of, in congenital syphilis, 67.
diseases of, cancer and other growths, 642.
celiac disease, 629.
constipation, 630.
diarrheal, of early childhood, 627.
dilatation of colon, 640.
diverticulum, 641.
enteritis, acute, 619.
enteritis, chronic, 623.
enteroptosis, 579.
obstruction, 633.
new growths of, 642.
polypoid growths of, 644.
sarcoma of, 644.
strangulation of, 636.
syphilis of, 34.
Intoxication impulse, 1175, 1177.
Intoxications, alcoholism, 1175.
arsenical poisoning, 1193.
beriberi, 1201.
carbon monoxid poisoning, 1196.
cocainism, 1187.
food poisoning, 1203.
lead poisoning, 1187.
mercurial poisoning, 1195.
morphinism, 1185.
pellagra, 1197.
Intra-esophageal stenosis, 566.
Intussusception, 637.
Invagination, 637.
Iodin, purpura from administration of, 543.
Iodothyroidism, acute, 1142.
Irritation of cervical sympathetic, 1082.
Ischemia, 514.
Ischio-rectal tuberculosis, 257.

J

Jacksonian epilepsy, 1055.
Jail fever. See Typhus Fever.
Jarisch-Herxheimer reaction, in syphilis, 21.
Jaundice, associated conditions of, 666-667.
black, 667.
catarrhal, 665.
chronic, prognosis of, 667.
deep, 666.
epidemic catarrhal, 350, 667.
hemo-hepatogenous, 668.
causes of, cerebral, 669.
infectious diseases, 669.
poisons and drugs, 669.

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Jaundice, hemo-hepatogenous, causes of, splenomegaly, 669.
sudden hemolysis, 669.
conditions indicated by, 669.
hemolytic, 668.
influence of spleen on, 668.
hepatogenous, causes of, 664.
hereditary splenomegalic, 670.
in cancer of liver, 709.
in cirrhosis, 692, 700.
infectious, 350.
in newly born, grave familial, 671.
infections, 671.
mortality from, 672.
obstructive, due to organic lesions in duct or liver, 671.
physiologic, 670.
in syphilis of liver, 30.
in typhoid fever, 105.
malignant, 673.
nature of, 664.
obstructive, 664.
primary diseases of, 666.
prognostic factors in, feces, 666.
urine, 665.
syphilitic, 670, 672.
toxic, 668.
with biliary colic, 721.
Joint complications, in amebic dysentery, 80.
Joints, diseases of, polyarthritis, destructive chronic, 1088.
hysterical, 1015.
intermittent dropsy of, 1079.
Juvenile paresis, 65.

K

Kahler's disease, 1134.
Kala-azar, 83.
Kidney, abscess of, 833.
amyloid, 814.
arteriosclerotic, 805.
benign growths of, 827.
congested, 811.
contracted, 805.
contracted granular, 804.
cyanosed, 811.
effect of, 813.
urine of, 813.
cysts of, 827.
diseases of, amyloid kidney, 814.
anomalies of urinary secretion, albuminuria, 741.
alkaptonuria, 786.
bacilluria (bacteriuria), 774.
casts, 749.
chyluria, 776.
cystinuria, 785.
hematoporphyrinuria, 787.
hematuria, 753.
indicanuria, 780.
lipaciduria, 787.
lipuria, 777, 787.
lithuria, 785.
melanuria, 786.
Kidney, diseases of, anomalies of urinary secretion, oxaluria, 779.
phosphaturia, 777.
pneumaturia, 787.
uremia, 762.
urobilinuria, 782.
congested kidney, 811.
movable, 828.
neoplasm, 825.
nephritis, acute parenchymatous, 788.
chronic interstitial, 804.
chronic parenchymatous, 797.
perinephric abscess, 834.
pyelitis, 829.
fibrosis of, 804.
floating, 828.
gouty, 804.
hydatid cysts of, 308.
hyperemia of, 811.
in scarlet fever, 331.
large white, 797.
malignant growths of, carcinoma, 825.
prognosis of, 826.
sarcoma, 825.
congenital, 826.
movable, 828.
neoplasm of, 825.
new growths of, hematuria with, 760.
papilloma of, 826.
polycystic, leading symptoms of, 827.
nature of, 827.
operation for, 827.
unilateral, 827.
pus in, 832.
drainage of, 834.
red granular, 805.
rupture of, hematuria with, 760.
secondary contracted, 797, 804.
senile, 805.
surgical diseases of, hydronephrosis, 815.
nephrolithiasis, 820.
syphilis of, 31.
waxy, 814.
Kidney complications, in gout, 1104-1105.
Kidney fixation, 828.
Kidney invasion, in arteriosclerosis, 411.
King's evil, 265.
Klebs-Loeffler Bacillus, 134.
Klumpke's paralysis, 877.
Korsakoff's psychosis, in alcoholic multiple neuritis, 849.
in alcoholism, 1182.
Kossel's conclusions, on tuberculosis, 219.
Kundrat's disease, 538.
Kussmaul, unrest of, in hypermotility, 617.

L

Labyrinthine disease. See Aural Vertigo.
Lactosuria, relation of, to diabetes, 1109.
Landry's paralysis, 322, 854.
Lardaceous disease, 814.
Laryngeal diphtheria, 136, 138.

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Laryngeal lupus, 252.
Laryngeal tuberculosis, and pulmonary, 251.
chronic, 251.
early recognition of, 251.
miliary deposit in, 251.
pregnancy in, 251.
primary, 250.
secondary process of, 250.
tendency to infiltration in, 250.
"tuberculoma" in, 251.
ulcerations in, 251.
Laryngismus stridulus, deaths from, due to status thymolymphaticus, 363.
in adults, 363.
in children, 362.
Laryngitis, acute, catarrhal, in children, 360.
factors in relief of, 361.
primary, 360.
catarrhal, in typhoid fever, 97.
causes of, 360.
chronic, 361.
associated conditions of, 361.
primary, 361.
edematous, 362.
in measles, 344.
secondary, 360-361.
spasmodic, 362.
syphilitic. See Syphilitic Laryngitis.
tuberculous, 234, 241, 251.
Laryngoscope, use of in edema of larynx, 362.
Larynx, diseases of, edema, 362.
laryngismus stridulus, 362.
laryngitis, acute, 360.
chronic, 361.
syphilitic. See Syphilitic Laryngitis.
tuberculous, 363.
edema of, causes of, 362.
laryngoscope in, 362.
Lateral and posterior disease, combined. See Ataxic Paraplegia, 901.
Lead encephalopathy, associated conditions of, 1190.
recurrence of, 1190.
symptoms of, 1189.
Lead multiple neuritis, 850.
Lead palsy, 1189.
Lead poisoning, acute, 1187.
arteriosclerosis due to, 406.
blood picture in, 1190-1191.
chronic, 1187.
chronic nephritis due to, 798.
colic of, 1188.
conditional symptoms with, 1188.
encephalopathy, 1189.
gout due to, 1101.
influencing factors in, age, 1188.
heredity, 1188.
sex, 1188.
occupational influence in, 1188.
palsy, 1189.
saturnine anemia in, 1190.
saturnine arteriosclerosis in, 1192.
Lead poisoning, saturnine arthralgia in, 1189.
saturnine nephropathy in, 1192.
with cerebral anemia, 948.
Lenticular degeneration, progressive, 695.
Leontiasis ossea, 1095.
Leprosy, anesthetic type of, 215.
history of, 214.
infection of, 214.
mixed type of, 216.
non-hereditary character of, 214.
period of incubation of, 214.
relapse of, 216.
sexual intercourse in, 215.
tubercular, fever in, 215.
skin and hair in, 214-215.
Wassermann reaction in, 215.
Leptomeningitis, 277.
purulent, as complication of disease, 938.
basilar, 939.
causes of, 938.
duration of, 942.
lumbar puncture in, 941.
metastatic, 938.
microörganisms causing, 938.
postbasilar, 939.
prognosis of, 939-940-941.
symptoms of, 939-940.
with metastatic parotitis, 939.
serous, chronic, 946.
hydrocephalus, acquired, 943.
congenital, 944.
serous meningitis, 943.
spinal. See Spinal Leptomeningitis.
symptoms of, in poliomyelitis, 323.
Leube rule, for early diagnosis of cancer, 603.
Leukanemia, 534.
Leukemia, acute, 534.
complications in, 535.
influence of treatment on prognosis of, 535.
leukanemia (Leube), 534.
leukocytic, blood picture of, 530.
definition of, 530.
myelocytic count in diagnosis of, 532.
symptoms of, 532.
cardiac, 532.
in final stages, 532.
priapism, 532.
splenic, 531-532.
urinary, 532.
lienal. See Leukemia, Leukocytic.
lymphatic, blood picture in, 533.
chloroma with, 533.
essential features of, 533.
symptoms of, 533.
mixed forms of, 535.
myelocytic. See Leukemia, Leukocytic.
myeloid. See Leukemia, Leukocytic.
remissions of, 535.
resemblance to, of lymphoblastoma, 537.
splenectomy in, 535.
splenomyelogenous. See Leukemia, Leukocytic.
transition of pseudo leukemia to, 541.

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Leukemia, x-ray in, 535.
Leukocythemia. See Leukemia, Lymphatic.
Leukocytosis, in appendicitis, 651.
Leukomain poisoning, 1203.
Leukoplakia buccalis, 555.
Lichtheim symptoms, of pernicious anemia, 520.
Lion face. See Leontiasis ossea.
Lipaciduria, 787.
Lipomata, of esophagus, 568.
Lips, tuberculosis of, 252.
Lipuria, 777, 787.
Lithuria, 785.
Little's disease. See Sclerosis, congenital lateral.
Liver, actinomycosis of, 302.
amyloid, 713.
amyloid degeneration of, in tuberculosis, 255.
and spleen, in tuberculosis, 234.
atrophy of, in syphilis, 30.
benign growths of, 711.
chancroid, 713.
circulatory disturbances of, congestion, 676.
diseases of hepatic artery, 680.
diseases of hepatic vein, 679.
diseases of portal vein, 678.
cirrhosis of, and tuberculosis, 255.
complicated by syphilis, 31.
enlargement of spleen with, 1171.
diseases of, abscess, 704.
acute yellow atrophy, 673.
amyloid, 713.
cancer, 709.
circulatory disturbances, 676.
cirrhosis, 681.
echinococcus. See Echinococcus Disease.
fatty, 712.
glucosuria due to, 1107.
jaundice, 664.
syphilis. See Syphilis of Liver.
tuberculosis. See Tuberculosis of Liver.
effect on, of malaria, 73, 74, 77.
enlargement of, in acute biliary colic, 722.
fatty degeneration of, 712.
in tuberculosis, 255.
fatty infiltration of, 712.
hydatid cysts of, 307.
hyperemia of, active, 676.
passive, 676.
in alcoholism, 1182.
lardaceous, 713.
multiple adenomata of, 711.
syphilis of, congenital, 30.
waxy, 713.
Liver abscess, causes of, 705.
due to cholelithiasis, 726.
due to infection, 704.
general considerations of, 704.
in amebic dysentery, 79.
Liver abscess, multiple, accompanying symptoms of, 707.
causes of, 707.
course of, 707.
secondary anemia and leukocytosis with, 708.
single or tropical, blood count in, 706.
complications in, 706.
course of, 707.
duration of, 705.
mortality from, 706.
primary diseases causing, 705.
rupture of, 706.
spontaneous cure of, 705.
without symptoms, 705.
Liver complications, in gout, 1105.
in typhoid fever, 105.
with endocarditis, 491.
Liver congestion, causes of, 676.
Liver flukes, 317.
Lockjaw. See Tetanus.
Locomotor ataxia. See Tabes dorsalis.
vertigo with, 869.
Locomotor system, bone diseases of, fragilitas ossium, 1097.
hypertrophic pulmonary arthropathy, 1096.
leontiasis ossea, 1095.
osteitis deformans, 1093.
joint diseases of, polyarthritis, destructive chronic, 1088.
muscular diseases of, akinesia algera, 1086.
myalgia, 1084.
myositis, 1084.
paramyoclonus multiplex, 1086.
progressive myositis ossificans, 1085.
Thomsen's disease (myotonia), 1085.
Ludwig's angina, 560.
causes of, 561.
definition of, 561.
mortality from, 561.
symptoms of, 561.
Lues. See Syphilis, 15.
Lues hereditaria tarda, 30-31.
Lues maligna, 20.
in syphilis of liver, 30.
Lumbago, 1084.
Lumbar neuralgia, 844.
Lumbar puncture, for brain parasites, 1002.
in brain abscess, 986.
in brain tumor, 998, 1000.
in encephalitis, 975.
in leptomeningitis, purulent, 941.
in poliomyelitis, 323.
in serous meningitis, 943.
in tumors of spinal cord, 926.
Lumbosacral paralysis, causes of, 879-880.
of anterior crural nerve, symptoms of, 880.
of external popliteal nerve, 881.
of gluteal nerves, 881.
of internal popliteal nerve, 881.
of obturator nerve, 880.

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Lumbosacral paralysis of sciatic nerve, 880.
Lung abscess, 386.
in influenza, 127.
in pneumonia 165.
in typhoid fever, 98.
Lung fever. See Pneumonia, Lobar.
Lungs, cirrhosis of, 379.
diseases of, abscess, 386.
cancer, 387.
congestion, 373.
emphysema, 382.
gangrene, 385.
hemorrhage, 376.
neoplasms, 387.
non-tuberculous pneumonia, 379.
fibrosis of, due to occupation, 380.
in pneumonia, 166.
gangrene of, in influenza, 127.
in pneumonia, 164.
hydatid cysts of, 308.
induration of, and endocarditis, 490.
neoplasms of, 387.
purulent infiltration of, in pneumonia, 166.
syphilis of, 33.
Lupus, of tongue and lips, 252.
Lymphadenitis, bronchial, 265.
cervical, 265.
Lymphadenoma. See Hodgkin's Disease.
Lymphangitis, due to filariasis, 316.
Lymphatic glands, tuberculosis of, 265.
Lymphatics, enlargement of, in congenital syphilis, 66.
Lymphatism, 1164.
Lymphemia. See Leukemia, Lymphatic.
Lymphocytoma, 537.
Lymphogranuloma. See Hodgkin's Disease.
Lymphosarcoma, 1164.
Lymphosarcomatosis, 538.
Lymph-scrotum, due to filariasis, 316.

M

Maidism. See Pellagra.
Malaria, black water fever, 76.
bronchitis with, 77.
cachexia in, chronic, 76-77.
from neglected treatment for, 76.
cause of lesions of, 72.
chronic cachexia in, 76.
complications in, 77-78.
enlargement of spleen in, 73.
factors in malignancy of, 73.
hemorrhagic, 76.
intermittent, 73.
irregular, 73.
quartan type of, 73.
quotidian type of, 73.
relapses of, 74.
spontaneous recovery from, 74.
tertian, 73.
miscarriages in, 78.
mixed types of, 77.
Malaria, neuralgia due to, 77, 839.
pigmentation of organs in, 72.
remittent, algid pernicious, 75.
black water disease, 76.
cerebral pernicious, 75.
coma type of, 75.
forecast in, 75.
gastro-intestinal pernicious, 75.
mania and convulsions in, 75.
manifestations of, 74-75.
paroxysms of, 74-75.
pernicious, 74.
pulmonary pernicious, 75.
purpuric complications in, 76.
specific origin of, 72.
Malignant granuloma. See Hodgkin's Disease.
Malignant growths, anemia due to, 515.
Malignant pustule. See Anthrax.
Malleus. See Glanders.
Malta fever, diagnosis of, by blood culture, 197.
etiology of, 196.
period of incubation in, 196.
prognosis of, 197.
symptoms of, 197.
Mania, in cerebral hemorrhage, 972.
in cerebral hyperemia, 951.
in malarial fever, 75.
suicidal, in morphinism, 1186.
with homicidal tendencies, in epilepsy, 1053.
Marie's disease, due to traumatism, 1090.
importance of early detection of, 1091.
prognosis of, 1091.
symptoms of, 1090.
tuberculosis with, 1090.
Marie's hereditary ataxia, 888.
Mastodynia, 843.
Maternity, tetany of, 1168.
Measles, complications in, brain, 345.
bronchitis, 344.
cancrum oris, 344.
diphtheria, 345.
ear, 344.
eye, 345.
gastro-enteritis, 345.
glandular, 345.
heart, 345.
pulmonary, 344.
scarlet fever, 345.
tuberculous meningitis, 345.
contagion of, 342.
German, 346.
malignant, 342.
mortality from, 344.
nature of, 342.
period of incubation of, 342.
period of invasion of, 342.
symptoms of, blood, 343.
conjunctiva, 343.
skin, 343.
temperature, 343.
urine, 343.
Median nerve paralysis, causes of, 878.
symptoms of, 878.

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Mediastinum, diseases of, associated symptoms of, 400.
tumors of, 399.
Mediastinopericarditis, 430.
Medulla oblongata, invasion of, in tabes dorsalis, 58.
Melanosis, 786.
Melanuria, 786.
Melena, in cirrhosis, 690.
Membranous colitis, hysterical, 1018.
Membranous croup, non-diphtheritic, Vincent's angina in, 298.
Ménière's disease. See Aural Vertigo.
Meningeal apoplexy, 930.
Meningismus, 931.
Meningismus typhosus, 111.
Meningitis, alcoholic, with alcoholic multiple neuritis, 849.
and epilepsy, 1055.
basilar, 224.
cerebrospinal, 932.
epidemic cerebrospinal, abortive cases of, 182.
blood picture of, 182.
character of, 177.
chronic cases of, 181.
complications in, 183-184.
factors influencing severity of, 179.
Flexner serum for, 184-185.
foudroyant cases of, 181.
general symptoms of, 179-180.
hydrocephalus due to, 181-182.
lumbar puncture in, 182-183.
mortality from, 177-178.
occurrence of, 178-179.
due to influenza, 129.
pneumococcus, 159.
postbasilar, 934.
purulent, with erysipelas, 176.
septic, 133.
serous, course of, 943.
diseases complicated by, 943.
primary, 943.
specific localized, in cerebral syphilis, 42.
spinal. See Spinal Meningitis.
tuberculous, 224, 242, 277.
with arthritis, 287.
with brain tumor, 994.
Meningo-encephalitis, 974.
and epilepsy, 1055.
Menstrual anomalies, hysterical, 1018.
in typhoid, 110.
palpitation of heart with, 508.
sudden anemia during, 515.
with tuberculosis, 271.
Mental anomalies, in cerebral hemorrhage, 971.
in chorea, 1040.
in diabetes mellitus, 1115.
in epilepsy, 1053.
in exophthalmic goiter, 1146.
in multiple sclerosis of brain and cord, 910.
in neurasthenia, 1031.
Mercurial poisoning, occupation influence in, 1195.
prognostic symptoms of, 1195.
Mesenteric tuberculosis, 266.
Metabolic faults, achondroplasia, 1131.
diabetes insipidus, 1122.
diabetes mellitus, 1106.
gout, 1098.
hereditary tendency to, 1125.
multiple myeloma, 1134.
obesity, 1124.
osteomalacia, 1131.
rachitis, 1129.
scorbutus, 1132.
Metastases, empyema with, 393.
in cancer of stomach, 606.
to brain, 990.
to spine and cord, 925.
due to carcinoma elsewhere in body, 919, 920.
Metastatic abscess of brain, 984.
Metastatic parotitis, 300.
Metasyphilitic disease, 44.
tabes dorsalis, 45.
Metazoan parasites, cestodes, 303.
nematodes, 309.
trematodes, 316.
Meteorism, in typhoid fever, 102.
Mexican tabardillo. See Typhus Fever.
Migraine, abortive, 1062.
classification of, 1060.
climacteric period in, 1060.
definition of, 1059.
exciting factors of, 1059.
hemicrania sympatheticotonica, 1062.
hemicrania sympatheticoparalytica, 1062.
influencing factors in, heredity, 1059.
infection and other toxic states, 1060.
traumatism, 1060.
tuberculosis, 1060.
various, 1060.
nature of, 1059.
ophthalmic, 1060-1061.
prognosis of, 1063.
red, 1062.
symptomatic, 1063.
symptoms of, general, 1059.
white, 1062.
with epilepsy, 1062.
with epileptic equivalent, 1062.
Mikulicz's disease, associated conditions of, 558.
Brunn's classification of, 557-558.
hereditary influence in, 558.
nature of, 557.
types of, 557.
Miliary eruption, in typhoid fever, 106.
Miliary tuberculosis, 222.
Milk, infected, epidemic tonsillitis due to, 294.
Milroy's disease, 1080.
Milzbrand. See Anthrax.
Mimic spasm. See Facial Spasm.
Miscarriages, in malaria, 78.
Mitral insufficiency, favorable cases of, 497.
unfavorable cases of, 497.
valvular lesions due to, 495.

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Mitral stenosis, cerebral embolism due to, 953.
hemoptysis of, 376.
of early life, 498.
unfavorable features of, 498.
valvular lesions due to, 497.
Mitral and tricuspid valves, insufficiency and stenosis of, 439.
Mobile spleen, 1173.
Mollities ossium, 1131.
Mononeuritis, 846.
Monoparalysis, hysterical, 1013.
Morphinism, accompanying conditions in, 1186.
course of intoxication in, 1185.
due to erythromelalgia, 1069.
effects of, 1185.
in tabes dorsalis, 54.
influencing factors in, bad heredity, 1186.
development of habit in medical students, 1186.
psychopathic states in, 1186.
quantity taken, 1185.
sudden complete withholding of drug from victim, 1185.
unstable nervous system, 1186.
percentage of permanent cures in, 1186.
prognosis of, 1185.
psychic anomaly in, 1185.
suicidal mania in, 1186.
Morvan's disease, 916.
Motor oculi, paralysis of, 860.
Mountain sickness, causes of, 1209.
dangers of, 1209.
prognosis of, 1209.
toleration in, 1209.
Mouth, diseases of, stomatitis, 553.
effect on, of typhoid fever, 101.
Mouth breathing, 299.
Movable kidney, associated symptoms of, 829.
operation for 828.
mortality following, 828.
prognostic factors of, 829.
Multiple myeloma, 1134.
of brain and cord, age considered in, 908.
apoplectiform seizures in, 910.
atypical types of, 911.
bulbar involvement in, 910, 912.
cause of, 909.
characterization of, 908.
complications in, 913.
course of, 908.
cutaneous reflexes in, 911.
diagnosis of, 911.
duration of, 911-912.
epileptiform attacks in, 910.
mental deterioration in, 910.
ocular changes in, 909, 910, 912.
periods of latency in, 909, 911, 912.
prognosis of, 911-912.
resemblance of, to transverse myelitis, 912.
scanning speech in, 910.
Multiple myeloma, of brain and cord, seats of predilection of, 908.
symptoms of, 909.
vertigo in, 910.
with ataxic symptoms in ascending, 912.
vertigo with, 869.
Mumps. See Parotitis, epidemic.
Muscles, diseases of, akinesia algera, 1086.
myalgia, 1084.
myositis, 1084.
paramyoclonus multiplex, 1086.
progressive myositis ossificans, 1085.
Thomsen's disease (myotonia), 1085.
Muscular atrophy in cerebral hemorrhage, 968.
Muscular dystrophy, complications of, 898.
course of, 896.
hereditary, 895.
juvenile, characteristics of, 897.
Erb-Landouzy-Déjérine, 897.
of childhood, atrophic, 897.
hypertrophic, 897.
pseudohypertrophic, 896.
prognosis of, 898.
progression of, 895.
symptoms of, 895.
Muscular rheumatism. See Myalgia.
Muscular spasm, in myotonia, 1085.
Muscular system in typhoid, 113.
Muscular weakness, in chorea, 1041.
in diabetes mellitus, 1116.
Musculospiral paralysis, causes of, 879.
common form of, 878.
complete, 878.
symptoms of, 879.
Musset's phenomenon, in exophthalmic goiter, 1144.
Myalgia, causes of, 1084.
lumbar, 1084.
occupation 1084.
prognosis of, 1084.
Myasthenia, 1030.
with chronic nephritis, 799.
Myasthenia gravis, associated conditions of, 894.
symptoms of, 893.
Mycosis intestinalis, 210.
Myelemia. See Leukemia, leukocytic.
Myelitis, acute, cervical, 906.
chronic stage on removal of cause of, 905.
compression or disorganization in, 905.
decubitus in, 905.
diffuse, 906.
due to traumatism, 905.
early symptoms of sepsis in, 905.
extent of paralysis in, 905.
foudroyant caseé of, 906.
lumbar cord involvement in, 906.
primary causes of, 905.
prognosis of, 905-906.
secondary, 905.
secondary to gonorrhea, 906.

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Myelitis, acute, syphilitic, 906.
transverse, 906.
with unrecognized cause, 906.
chronic, associated diseases of, 907.
causes of, 907.
compression, 907.
of pregnancy, 907.
periods of latency in, 907.
prognosis of, 907.
classification of, bulbar, 904.
central, or poliomyelitis, 904.
diffuse or general, 904, 906.
due to influenza, 130.
focal, 904.
transverse or compression, 904, 906, 907.
unilateral, 904.
compression, in tumors of spinal cord, 925.
definition of, 904.
funicular, 927.
post-typhoid, 112.
subacute, 905, 907.
transverse, from extradural tumors of cord, 925.
resemblance to, of multiple sclerosis, 912.
tuberculous, 277.
Myelocytes, in leukemia, leukocytic, 530.
Myeloma, multiple, 1134.
Myelopathic albumosuria, 1134.
Myocardial degeneration, 443.
in amebic dysentery, 80.
in arteriosclerosis, 412.
in scarlet fever, 330.
Myocardial insufficiency, angina pectoris, 454.
blood pressure study in, 445.
brown atrophy, 454.
chronic, cause of, 443.
complex conditions in, 444-445-446.
depressing factors from, 452.
factors in prognosis of, 444-445-446.
fatty heart, 452.
fibroid degeneration, 443.
irregularities of, auricular fibrillation, 450.
due to depressed conductivity, 447.
due to extrasystoles, 448.
pulsus alternans, 449.
sinus, 447.
Windle's table of, 450.
nature of, 443.
sudden death from, 446.
symptoms of, 444-445-446.
coronary sclerosis, 454.
fragmentation and segmentation, 454.
in cirrhosis, 700.
senile heart, 460.
with anemias, metabolic faults, and toxic states, 465.
Myocarditis, acute interstitial, septic, 443.
simple, 443.
acute purulent, 442.
associated with pericarditis, 428.
due to arthritis, 285.
Myocarditis, due to arthritis, blood pressure in, 286.
sudden death from, 286.
due to syphilis, 29.
in chorea, 1042.
in diphtheria, 139.
parenchymatous, 443.
post-typhoid, 95.
with cholelithiasis, 731.
Myocarditis hemorrhagica, 1085.
Myocardium, diseases of, aneurism, 467.
chronic insufficiency, 443.
fibroid degeneration, 443.
heart weakness due to insufficient exercise, 464.
hypertrophy and dilatation, 460.
inherent muscular weakness, 465.
insufficiencies with anemias, metabolic faults and toxic states, 465.
myocarditis, acute interstitial, 443.
myocarditis, acute purulent, 442.
neoplasms, 465.
rupture, 466.
Stokes-Adams disease, 463.
syphilis. See Cardiovascular syphilis.
influence of, on prognosis, 441.
obesity with, 1126.
parasites of, 466.
tuberculosis of, 275.
Myoclonia, 1086.
Myogenic hypothesis, of paralysis agitans, 1035.
Myositis, 32.
Myositis ossificans, progressive, 1085.
Myotonia, 1085.
Myotonia congenita, 898.
Myotonic reaction of Erb, 1086.
Myxedema, adult, 1156.
prognosis of, 1157.
symptoms of, 1156-1157.
classification of, 1154.
congenital, prognosis of, 1156.
symptoms of, 1155.
thyroid treatment for, 1156.
due to complete loss of gland function, 1157.
heredity in, 1158.
in exophthalmic goiter, 1147.
operative, 1154.
prognosis of, 1158.
thyroid insufficiency in, 1153.
thyroid insufficiency in, dangers of, 1154.
maximal, 1154.

N

Narcotic poisoning, double, with alcoholism, 1178.
Nasal diphtheria, 138.
Nasal tuberculosis, 250.
Naso-pharyngeal obstructions, 299.
Necator americanus of Stiles, 310.
Neisser's Statistics, on tertiary syphilis, 25.

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Nematodes, ankylostomiasis, character of, 310.
clinical manifestations of, 311.
incidence of, 311.
infection of, 310.
occurrence of, 310.
prognosis of, 311.
ascaris lumbricoides, 309-310.
filariasis, 314-315.
oxyuris vermicularis, 309-310.
trichinosis, cause of, 312.
duration of, 315.
factors in prognosis of, 313.
infection of, 312.
mortality from, 315.
symptoms of, blood, 314.
intestinal, 313.
respiratory, 313-314.
trichocephalus dispar, 312.
Neoplasms, pancreatic, 739.
pulmonary, 387.
thyroid, 1136.
and hyperthyroidea, 1150.
Neoplasms of esophagus, 567.
Neoplasms of heart, primary, 465.
secondary or metastatic, 466.
Neoplasms of pericardium, 434.
Neoplasms of peritoneum, 663.
Nephritis, acute, complications in, 794.
glomerular type of, 789.
mortality from, 793-794.
symptoms in prognosis of, 790.
alluminuria, 793.
blood, 793.
cardiac, 791.
peritonitis, 792.
pulmonary edema, 792.
uremia, 792.
urinary, 791.
vomiting, 792.
acute croupous, 788.
acute non-suppurative, of Councilman, 789.
acute parenchymatous, 788.
in typhoid, 108-109.
acute syphilitic, 790.
acute tubal, 788.
indicated by hematuria, 756.
aggravation of, by pregnancy, 796.
albuminuria and, 743, 744, 793.
albuminuria of, in typhoid, 108.
alcoholism with, 1180.
and appendicitis, 657.
benign, albuminuria in, 741.
chronic, arteriosclerosis with, 802.
coronary disease with, 802.
due to bacillary dysentery, 196.
duodenal ulcer with, 588.
chronic catarrhal, 797.
chronic diffuse, 797.
chronic interstitial, Adams-Stokes phenomenon in, 807.
albuminuric retinitis in, 809.
anemia in, 809.
angina pectoris in, 807.
arteriosclerotic kidney, 805.
Nephritis, chronic interstitial, blood pressure in, 806.
cerebral hemorrhage with, 958.
cerebral symptoms in, 807.
complications in, 809.
contracted kidney in, 805.
digestive symptoms in, 808.
dropsy in, 807.
duration of, 810.
dyspnea in, 807.
epistaxis in, 809.
headache in, 806-807.
heart changes in, 806-807.
hemoptysis of, 377.
heredity in, 805.
hypertension in, 806-807-808.
hypertrophy of left ventricle in, 806.
indicated by hematuria, 756.
infections in, 80.
in lead poisoning, 1192.
leading features of, 804.
ocular disturbances in, 806-807.
orthopnea in, 807.
polyuria in, 807.
prognosis of, 805.
purpura in, 809.
red granular kidney, 805.
renal insufficiency in, 806.
respiratory symptoms in, 807.
secondary contracted kidney, 804.
senile kidney, 805.
stasis in, 807.
surgical operations in, 809.
tachycardia in, 807.
thick artery in, 806.
urine in, 808.
with cholelithiasis, 730.
chronic parenchymatous, 797.
anemia with, 799.
arteriosclerosis in, 802.
associated conditions of, 797.
blood pressure in, 801.
compensatory hypertension in, 802.
compensatory hypertrophy in, 797, 802.
complications in, 803.
coronary disease with, 802.
digestive derangement with, 798.
due to chronic lead poisoning, 798.
due to cold or exposure, 798.
due to malarial infection, 798.
duration of, 804.
edema in, 802.
faulty living in, 802.
following nephritis of scarlatina, and pregnancy, 798.
immediate causes of death from, 804.
myasthenia with, 799.
origin of, 798.
paroxysmal hematuria with, 801.
process of, 797.
prognosis of, 797, 798, 803.
prolonged surgical conditions, associated with, 789.
pulse in, 802.
renal sufficiency test for, 800.

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Nephritis, chronic parenchymatous, retinal changes in, 803.
surgical treatment in, 804.
uremia with, 799.
urine in, 800.
vomiting with, 798.
chronic tubal, 797.
indicated by hematuria, 756.
diffuse interstitial, 873.
hematuria due to, 754-755.
in measles, 345.
in syphilis, 31.
interstitial, with cholelithiasis, 730.
in pneumonia, 160.
in varicella, 342.
of pregnancy, 794.
albuminuria in, 794.
diet and treatment for, 795.
eclampsia in, 795.
mortality from, 795.
prognostic factors in, 795.
post febrile, in typhoid, 109.
renal asthma with, 370.
saturnine chronic, retinal hemorrhage with, 798.
scarlatinal, 331.
septic, 131.
suppurative, 833.
tuberculosis, hematuria due to, 759.
tubular, renal sufficiency test for, 769.
urinary casts with, 750-751-752.
vascular, renal sufficiency test for, 769.
with arteriosclerosis, 411, 802.
with cirrhosis, 685.
with diphtheria, 139.
with endocarditis, 491.
with malaria, 78.
Nephrolithiasis, calculous anuria in, 824.
cause of, 820.
conditions associated with, 823-824.
diathesis in, 823.
mortality following operations for, 824.
operation for (nephrolithotomy), 824.
prognostic features of, 821.
reaction of urine in, 821.
renal colic in, 823.
renal lithiasis in, 823.
size and number of stones in, 821.
stone in pelvis of kidney in, 822.
symptoms of, 823-824.
ureteral stones in, 822.
varieties of, 821.
x-ray in, 821.
Nephropathies, acute, duration of, 793.
infectious history of, 790.
amyloid kidney, 814.
chronic, 797.
complications in, 803.
dropsy in, 800.
nephritis, chronic interstitial, 804.
congested kidney, 811.
malignant toxemia in, 788.
nephritis, acute parenchymatous, 788.
non-malignant toxemia in, 789.
origin of, 788.
prognostic factors in, 788.
Nephropathies, saturnine, 1192.
symptoms of, 788-789.
tuberculous kidney. See Tuberculous kidney.
Nephroptosis, associated symptoms of, 828.
Dietl's crises in, 829.
hydronephrosis with, 829.
operation for, 828.
mortality following, 828.
prognostic factors in, 829.
Nephrotyphoid, 108.
Nerves, anterior crural, paralysis of, 880.
auditory, paralysis of, 868.
brachial, paralysis of, 875-876.
cauda equina, paralysis of, 882.
circumflex, paralysis of, 878.
cochlear, invasion of, in auditory paralysis, 868.
gluteal, paralysis of, 881.
hypoglossal, paralysis of, 873.
median, paralysis of, 878.
musculospiral, 878.
obturator, paralysis of, 880.
peripheral, tumors of, 883.
phrenic, paralysis of, 874.
popliteal, paralysis of, 881.
sacral, paralysis of, 882.
sciatic, paralysis of, 880.
spinal accessory, paralysis of, 871.
ulnar, paralysis of, 879.
vestibular, involvement of, in auditory paralysis, 869.
Nervous dyspepsia of Leube, 574.
Nervous exhaustion. See Neurasthenia.
Nervous prostration. See Neurasthenia.
Nervous system, anomalies of, in malaria, 78.
complications of, in gout, 1104.
diseases of, anterior—of efferent or motor tract, 888.
brain parasites, 1002.
cerebellar disease, 1003.
circulatory disturbances of brain, 947.
of brain membranes, 934.
of spinal membranes, 930.
peripheral, neuralgia, 837.
neuritis, 845.
paralysis, 856.
tumors, 883.
sympathetic, 1081.
diseases of spinal cord, indiscriminate, 904.
lateral, 899.
of afferent or sensory system, 885.
diseases of sympathetic system, vasomotor and trophic disturbances, 1066.
effect on, of congenital syphilis, 67.
functional and general diseases of, chorea, 1037.
epilepsy, 1046.
hysteria, 1005.
infantile convulsions, 1065.
migraine, 1059.
neurasthenia, 1025.

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Nervous system, functional and general diseases of, occupation paralysis and neurosis, 1064.
paralysis agitans, 1033.
tetany. See Tetany.
traumatic neurosis, 1021.
functional heart disorders due to, 507.
in alcoholism, 1181.
in cholelithiasis, 732.
in diabetes mellitus, 1118.
in endocarditis, 492.
influenza of, 129.
in typhoid, 111.
in tuberculosis, 235.
invasion of, in amebic dysentery, 80.
in cirrhosis, 694.
in pellagra, 1200.
in pneumonia, 158.
symptoms of, in exophthalmic goiter, 1143-1146.
syphilis of, 35.
tuberculosis of, 277.
Neuralgia, age in, 838.
arteriosclerotic, 842.
brachial, 843.
brachial, 843.
associated conditions of, 843.
causes of, 843.
ciliary, 841.
climate considered in, 838.
conditions indicated by, 844.
conditions responsible for, 837.
crural, 840, 844.
definition of, 837.
due to anemia, 838.
due to bad habits, 839.
due to cachexias, 839.
due to caries of teeth, 840.
due to diabetes, 839.
brachial, 843.
due to infections, 839.
due to malaria, 839.
due to poisons, 839.
due to syphilis, 839-840.
due to tumors of spinal cord, 921.
epidemics of, 839.
"fixed," 840.
hyperesthetic areas of Head in, 840.
idiopathic, 837.
intercostal, conditions indicated by, 842.
lumbar, 844.
persistent double, 844.
malarial, 77.
mastodynia, 843.
mild paroxysms of, 840.
occipital, conditions indicated by, 841.
persistent or recurring, in extremities, 840.
phrenic, 843.
predisposition to, 838.
red. See Erythromelalgia.
relapses of, 841.
sex in, 838.
sciatic, 844.
acute idiopathic, 845.
causes of, 845.
chronic neuritic, 845.
Neuralgia, sciatic, conditions symptomatic of, 844.
double, 845.
neuropathic tendency of, 844.
results of long-continued, 845.
subacute secondary, 845.
symptomatic, prognosis of, 845.
senile, 842.
supra-orbital, causes of, 841.
treatment for, 842.
symptomatic, 837.
intercostal, 843.
with flabby and atrophic muscles, 840.
with transitory tenderness, 840.
trifacial, 841.
associated symptoms of, 841.
causes of, 841.
Neuralgia of stomach, 616.
Neuralgic pains, about head and jaw, 840.
due to incipient brain disease, 840.
nasal and frontal, 840.
of herpes zoster, 885-886.
persistent or recurring, in abdomen, 840.
in thorax, 840.
radiating along intercostal, and lumbar nerves, 839.
with hysteria, 841.
Neurasthenia, age in, 1026, 1032.
"anxiety neurosis" of Freud, 1029.
associated conditions of, cardiac neuroses, 1027.
gastro-intestinal disturbances, 1027.
infections, 1027.
influenza, 1027.
traumatism, 1027.
aural symptoms of, 1030.
"brain fag" in, 1031.
cardiac neurosis in, 1029.
causes of, faulty hygiene with improper education, 1027.
high altitudes, 1026.
idleness, 1026.
insufficient early discipline, 1026.
occupation, 1027.
cerebral, 1028.
clinical varieties of, 1028.
constipation with, 1031.
coöperation of physician and patient in, 1032.
course of, 1032.
definition of, 1025.
due to alcoholic history, 1027.
due to diabetic history, 1027.
due to gouty history, 1027.
due to influenza, 129.
dyspepsia due to, 615.
emaciation with Glénard's process in, 1031.
exogenous nature of, 1026.
factors influencing course of, 1029.
faulty nutrition in, 1031.
fear and imagination in, 1030.
gastro-intestinal anomalies in, 1031.
heart complaints of, 513.
history of, 1025.
inherent weakness in 1032.

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Neurasthenia, insanity due to psychasthenic states in, 1030.
melancholy of, 1028.
Ménière symptoms in, 869.
mental character in, 1025.
muscular weakness in, 1030.
ocular symptoms in, 1030-1031.
operative treatment for varicocele in, 1029.
phobias of, 1030.
predisposition by heredity to, 1026, 1028.
predisposition of race to, 1026.
primary, 1025.
reflexes in, 1030.
removal of cause of, 1032.
secondary nature of, 1025.
sensory symptoms in, 1030.
sex in, 1026.
sexual, 1028-1029.
spinal, 1028.
urinary anomalies in, 1029.
Neurasthenic habits, 1030.
Neuritis, bulbar, acute, 892.
due to influenza, 129.
in pneumonia, 168.
in rheumatic fever, 287.
multiple, symptoms of, in poliomyelitis, 323.
tuberculous, 278.
optic, 858.
peripheral. See Peripheral Neuritis.
sciatic, 844.
syphilitic peripheral, 37.
tuberculous, 278.
Neuritis-polyneuritis, 1119.
Neurofibromata, disseminated, with central deposits, 883.
chronic, 883.
congenital, 883.
involving subcutaneous branches of sensory nerves, 884.
multiple, 883.
plexiform, 884.
size of, 883.
symptoms of, 883.
Neuromata, false, 883.
following amputation, 883.
true, 883.
Neuropathic predisposition, 838.
Neurorecidive, polyneuritis due to salvarsan, 852.
Neurosis, traumatic, 1021.
Noma, 555.
Nose, diseases of, acute catarrhal rhinitis, 357.
hay fever, 358.
effect on, of congenital syphilis, 66.
syphilis of, 32.
Nosebleed. See Epistaxis.
Nutrition, disordered, in epilepsy, 1052.
faulty, in neurasthenia, 1031.
with cerebellar disease, 1004.
Nystagmus, in ophthalmoplegia, 861.

O

Obesity, acquired, causes of, 1125.
treatment for, 1125.
age considered in, 1126.
cardiac insufficiency and death due to, 1125.
causes of, 1124.
change by decomposition and reformation of fat deposits, 1126.
complications in, acute hemorrhagic pancreatitis with, 1127.
amenorrhea, 1128.
angina pectoris, 1127.
arteriosclerosis with myocardial change, 1127.
cardiac asthma, 1127.
constipation with hemorrhoids, 1127.
dropsy, 1128.
dystrophia adiposo-genitalis in, 1128.
emphysema with bronchitis and insufficient heart muscle, 1127.
in asthenic or anemic cases, 1128.
interference with locomotion, 1127.
interstitial nephritis, 1127.
myocardial insufficiency, 1127.
plethora, 1127.
constitutional inclination to, 1126.
dangers of, 1126.
thyroid extract in large doses, 1128.
unscientific dieting in, 1128.
diabetes mellitus with, 1112.
effect of relief of sexual anomalies on, 1125.
fatty degeneration of myocardium in, 1125.
fatty heart with, 1126.
heart weakness in, 1126.
hereditary, 1125.
at menopause, 1125.
at puberty, 1125.
hypoplasia in, 1128.
in anemic subjects, 1125.
in tuberculosis, 242.
poor insurance risks, 1128.
poor surgical subjects, 1128.
pregnancy in, 1128.
prognosis of acute infections in, 1126.
sudden death from, 1127-1128.
treatment for, 1128.
tumor of hypophysis in, 1128.
Obstipation, in appendicitis, 653.
organic causes of, 631.
Obturator nerve, paralysis of, 880.
Occipital neuralgia, 842.
Occupation, arteriosclerosis due to, 407-408.
Occupation diseases, pneumonia, 380-381.
Occupation neuroses, 1064.
Occupation paralyses, chronic, 1064.
pathologic basis for, 1064.
relief from, 1064.
symptoms of, 1064.
ulnar, 879.
various, 1064.
writers' cramp, 1064.

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Ocular anomalies, hysterical, amblyopia, 1012.
asthenopia, 1012.
blindness, 1012.
contraction of visual field, 1011.
contracture of ocular muscles, 1013.
errors of accommodation, 1012.
faulty color perception, 1012.
palpebral and bulbar, 1013.
paralysis of eyelids, 1013.
paralysis of ocular muscles, 1013
pupillary phenomenon, 1013.
due to alcoholism, 1183.
in arteriosclerosis, 415-418.
in chorea, 1040.
in chronic interstitial nephritis, 806-807.
in epilepsy, 1051.
in lead encephalopathy, 1190.
in neurasthenia, 1030-1031.
supra-orbital neuralgia due to, 841.
with hydrocephalus, 945.
Ocular infections, with diabetes mellitus, 1119.
hysterical paralysis of, 1013.
Ocular nerves, paralysis of, 860.
in tabes dorsalis, 56.
Olfactory nerve, paralysis of, 856.
Oligemia, 514.
Oligochromemia, 514-517.
Oligocythemia, 514.
in chlorosis, 518.
Ophthalmic migraine, 1060.
of Charcot, 860.
Ophthalmoplegia, 861.
acute, 862.
associated symptoms of, 861.
in tabes dorsalis, 56.
nystagmus in, 861.
recurrent, 862.
Ophthalmoscopic examination, in cerebral hemorrhage, 966.
in otitic brain abscess, 984.
Opium, enteritis due to, 625.
Oppenheim's disease, 898.
Optic aphasia, 859.
Optic changes, in multiple sclerosis of brain and cord, 909, 910, 912.
Optic nerve, atrophy of, 858.
in tabes dorsalis, 54.
hereditary family, 858.
with brain tumor, 994-995.
disseminated sclerosis of, 858.
paralysis of, 857.
Optic neuritis, conditions indicated by, 858.
syphilitic, 43.
with brain tumor, 994-995.
with cerebellar disease, 1004.
Oral sepsis, provocative of pernicious anemia, 527.
Orchitis, in typhoid, 110.
Orthopnea, in nephritis, 807.
Osler's disease. See Erythremia.
Osseous system, in typhoid, 113.
Osteitis deformans, duration of, 1095.
malignant growths with, 1094.
pathology and symptoms of, 1093-1094.
skull involvement in, 1094.
Osteoarthropathy, hypertrophic pulmonary, 1096.
Osteochondritis syphilitica, 67.
Osteogenesis imperfecta, 1097.
Osteomalacia, characteristics of, 1131.
early recognition and treatment of, 1132.
puerperal, 1132.
symptoms of, 1132.
uncontrolled cases of, 1132.
Otitis, brain abscess following, 983.
cerebral thrombosis due to, 955.
Otitis media suppurativa, diphtheria in, 142.
in measles, 344.
in pneumonia, 167.
Ovarian tuberculosis, 272.
Oxalic acid diathesis, 779.
Oxaluria, 779.
Oxyuris vermicularis, 309-310.

P

Pachymeningitis, cervical hypertrophic, with syringomyelia, 917.
hypertrophic cervical, 932.
spinal. See Spinal Pachymeningitis.
tuberculous, 277.
Pachymeningitis externa, development of, 937.
nature of, 936.
primary and secondary, 937.
prognosis of, 937.
Pachymeningitis interna, acute hemorrhagic, 931.
paresis with, 935.
causes of, 935-936.
chronic form of, 936.
development of, 935-936.
due to chronic alcoholism, 935.
due to infections, 936.
due to purpuric conditions, 935.
due to syphilitic infections, 936.
due to traumatism, 934-935.
general considerations of, 934.
prognosis of, 935.
senile dementia with, 935.
symptoms of, 935-936.
Pachymeningitis spinalis hemorrhagica, 930.
Paget's disease. See Osteitis deformans.
Pains, hysterical, simulating organic disease, 1010.
Palsies. See Paralysis.
Paludism. See Malaria.
Pancreas, cancer of head of, 739.
simulation of, by gall-stones, 730.
diseases of, calculi, 738.
cysts, 738.
hemorrhage, 737.
necrosis, 738.

Digitized by Google

Pancreas, diseases of, neoplasms, 739.
pancreatitis, 734.
relation of, to diabetes mellitus, 1106.
sclerosis of head of, 737.
tuberculosis of, 262.
with cholelithiasis, 731.
with diabetes mellitus, 1106.
Pancreas-achylia, functional, 625.
Pancreatic apoplexy, 737.
Pancreatitis, acute, gall-stone provoking factor of, 734.
acute hemorrhagic, 734.
due to traumatism, 735.
Cammidge test for, 736.
chronic, associated conditions of, 737.
causes of, 736.
hemorrhagic gangrenous, 735-736.
hemorrhagic, hiccough with, 875.
secondary, 736.
suppurative, 736.
Papilloma of kidney, 826.
Parageusia, 870.
Paralysis, anterior crural, 880.
auditory, 868.
bulbar, 891.
cerebral, of childhood, 977.
circumflex, 878.
crossed, hypoglossal and hemiplegia, 874.
crossed facial, with hemiplegia, 866.
deaths from, and apoplexy, table of, 959.
diphtheritic, 140.
Duchenne, 877.
due to cervical rib, 876.
Erb's, 876.
extensor, in lead multiple neuritis, 851.
facial, 847, 863.
due to pontine disease, 864.
glossopharyngeal, 870.
habit, 847.
hysterical, 1013.
influence of traumatism on development of, 1024.
infraclavicular, 877.
Klumpke's, 877.
Landry's, 854.
lumbosacral, 879.
musculospiral, 878.
obstetrical, 978.
ocular, 860.
in tabes dorsalis, 56.
of cauda equina, 882.
of cervical sympathetic, causes of, 1081.
prognosis of, 1081.
symptoms of, 1081.
of external popliteal nerve, 881.
of eyelids, hysterical, 1013.
of fifth (trigeminal) nerve, 862.
of fourth (trochlear) nerve, 861.
of gluteal nerves, 881.
of hypoglossal nerve, 873.
of internal popliteal nerve, 881.
of median nerve, 878.
of nerves of brachial plexus, 875-876.
of obturator nerve, 880.
of phrenic nerve, 874.
of posterior thoracic nerve, 877.
of sacral plexus, 882.
Paralysis, of serratus magnus, 877.
of seventh (facial) nerve, 863.
of sixth (abducens) nerve, 861.
of spinal accessory nerve, 871.
of sternomastoid, 872.
of third nerve (motor oculi), 860.
ophthalmoplegia in, 861.
peripheral. See Peripheral Paralysis.
peripheral facial, 864.
pneumogastric, 871.
pseudobulbar, 893.
quadriplegia, due to alcoholic multiple neuritis, 849.
radial, 878.
rheumatic facial, 848.
sciatic, 880.
spastic, 899.
spastic family type of, associated with idiocy, 903.
subscapular, 877.
supraclavicular, 876.
trapezius, 872.
ulnar, 879.
vagus, 871.
with cerebral anemia, 948.
with cerebral hemorrhage, 968.
with cerebral thrombosis, 956-957.
Paralysis agitans, age in, 1033-1034.
arteriosclerosis with, 1033.
complications in, bed-ridden cases, 1036.
fractures and other trauma, 1036.
infections, 1036.
nervous, 1036.
course of, 1035.
factors in prognosis of, 1034.
frequency of, 1034.
general symptoms of, 1033.
heredity in, 1034.
in tabes dorsalis, 58.
inviting factors of, 1034.
juvenile forms of, 1033.
mental condition in, 1036.
myogenic hypothesis of, 1035.
parathyroid therapy, 1035.
pathogenesis and pathology of, 1034.
periods of latency in, 1036.
premature decay in, 1033.
sex in, 1034.
symptoms of, facial expression, 1036.
hold of hand and arm, 1036.
muscular rigidity, 1035.
reflexes, 1036.
sphincter, 1036.
stooping posture, 1036.
"trotting gait," 1036.
tumor, 1035.
Paralysis chiropodale, due to arsenical multiple neuritis, 852.
Paramyoclonus multiplex, 1086.
Paranephritic abscess, 834.
Paranephritis, 834.
Paraplegia, ataxic, 901.
secondary spastic, causes of, 903.
course of, 902.
senile, 929.
spastic. See Sclerosis, primary lateral.

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Paraplegia, sudden, with embolism of cord, 929.
Parasites, intestinal, in beriberi, 1201.
of brain 1002.
metazoan, 303.
Paratyphlitis, 644.
Paratyphoid disease, bacilli of, 122.
complications in, 123.
puerperal, 124.
relapses of, 123.
symptoms of, 123.
Parathyroid disturbance, tetany of, 1168.
Parathyroid therapy, in paralysis agitans, 1035.
Paresis, and pachymeningitis interna, 935.
as syphilitic lesion, 35.
average duration of, 62.
causes of death in, 64.
choreatic, 980.
effect of treatment in, 64.
juvenile, 65.
manifestations of, 63-64.
periods of latency in, 63.
predisposing factors to, 62.
prevention of, in syphilis, 39.
remissions in, 63.
simulation of symptoms of, in cerebral lesions, 63.
trophic changes in, 63.
Wassermann reaction in, 63.
Parkinson's disease. See Paralysis agitans.
Parosmia, causes of, 857.
Parotid tuberculosis, 249.
Parotitis, chronic, 557.
epidemic, complications in, 353.
mortality from, 353.
nature of, 352.
symptoms of, 353.
in gastric ulcer, 596.
in typhoid fever, 101.
infectious, 300.
metastatic, 300.
in pneumonia, 168.
with erysipelas, 176.
secondary, 300.
with diphtheria, 142.
Parry's disease, 1142.
Pasteur treatment, of hydrophobia, 355.
"Patchy tongue," 555.
Pellagra, acute and subacute, 1199.
associated symptoms of, 1197.
chronic, 1199.
etiology of, 1198.
geographical distribution of, 1197.
origin of, 1197.
prognostic factors and symptoms in, 1198.
age, 1199.
central and peripheral lesions, of nervous system, 1200.
course of, 1199.
gastro-intestinal, 1200.
habits, 1199.
location, 1199.
psychic disturbances, 1200.
race and sex, 1200.
skin lesions, 1200.
Pelvis, pus in, 832.
Pemphigus syphiliticus, early, 66.
Peptic ulcers, of esophagus, 564.
Perforating ulcer, in tabes dorsalis, 57.
Perforation of intestine, in amebic dysentery, 80.
Peri-arteritis, 402.
Pericardial pseudocirrhosis of liver, 432.
Pericarditis, acute, adhesions of, 428.
and diphtheria, 140.
and endocarditis, 489.
and myocarditis, 428.
definition of, 426.
effusions of, blood stained, 428.
fibrinous, 428.
purulent, 428.
serofibrinous, 428.
in chorea, 1042.
in pneumonia, 166.
in typhoid fever, 96.
mortality from, 427, 430.
primary infections of, 426-427.
prognostic significance of, 427.
associated conditions of, general, 429.
valvular, 430.
calcareous, 428.
chronic, 430.
due to arthritis, 285.
idiopathic, 427.
prognosis of, 429-430.
symptoms of, 429.
tuberculous, 274.
x-ray examination in, 428.
Pericardioperitonitis, chronic, associated conditions of, 432-433.
character of, 432.
symptoms of, 432-433.
Pericardium, adherent, 430.
diseases of, adherent pericardium, 430.
hemopericardium, 433.
hydropericardium, 433.
neoplasms, 434.
pericardioperitonitis, 432.
pericarditis, 426.
pneumopericardium, 434.
Perigastric adhesions, in gastric ulcer, 595.
Perihepatitis, ascites with, 702.
associated symptoms of, 701.
chronic hyperplastic, 702.
fatal terminations of, 703.
tapping in, 702.
Perinephric abscess, definition of, 834
definition of, 829.
due to kidney disease, Guiteras' classification of, 835.
in renal tuberculosis, 269.
nature of primary lesion of, 835.
occurrence of, 836.
origin of, 835.
perforation of, 836.
primary case of, 836.
prognostic factors in, 835.
timely recognition of, 835.
Perinephritis, 835.
Perineuritis, 846.

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Peripheral nerves, elephantiasis neuromatosa, 884.
neuralgia, 837.
neuritis, 845.
paralysis, 856.
tumors of, benign solitary, 883.
malignant, 883.
neurofibromata, 883.
neuroma, 883.
Peripheral neuritis, chronic and progressive forms of, 846.
degenerative changes in, 846.
diabetic. See Diabetes Mellitus.
general considerations on, 845.
habit paralysis in, 847.
Landry's paralysis, classification of, 854.
complications in, 854.
mononeuritis, 846.
multiple, 846.
causes of, 848.
forms of, 848.
with leprosy. See leprosy.
multiple alcoholic, 849.
acute, of ascending type, 850.
in delirium tremens, 849.
Korsakoff's psychosis in, 849.
meningeal symptoms in, 849.
quadriplegic paralysis due to, 849.
with myocarditis, 850.
multiple arsenical, acute and chronic, 852.
associated symptoms of, 852.
bulbar symptoms with, 853.
causes of, 852.
complications in, 853.
due to salvarsan, 852.
paralysis with, 852.
pseudotabetic symptoms with, 852.
trophic symptoms of, 853.
multiple gonorrheal, 855.
multiple idiopathic, associated symptoms of, 853.
infections, 853.
prognosis of, 853.
reaction of degeneration in, 854.
temperature in, 853.
types of, 853.
multiple lead, 850.
in children, 851.
chronic, 851.
encephalopathy in, 851.
partial recovery from, 851.
reaction of degeneration in, 851.
relapses of, 851.
severity of poisoning in, 851.
multiple, postdiphtheritic. See Diphtheria, Paralysis.
multiple puerperal, 854.
preaxial, of Gombaults, 846.
prognosis of, 846.
reaction of degeneration in, 847.
secondary forms of, origin of, 845.
single, 846.
acute, 848.
course of, 846.
due to exposure to cold, 847.
Peripheral neuritis, single, due to infections, 847.
due to occupation palsies, 847.
due to pressure of crutches, 847.
postoperative, 848.
prognosis of, 846-847.
secondary, 847.
syphilitic, 37.
traumatic single, 846.
tuberculous. See Tuberculous neuritis.
Peripheral paralysis associated with cerebral and spinal lesions, 856.
brachial, 875.
circumflex, 878.
due to cervcal rib, 876.
infraclavicular, 877.
median, 878.
musculospiral, 878.
of posterior thoracic nerve, 877.
supraclavicular, 876.
ulnar, 879.
cauda equina, 882.
cause of, neuritis, 856.
cervical, hiccough-spasm of diaphragm in, 875.
cervical, phrenic, 874.
cranial, of auditory nerve, 868.
Bell's palsy, 864.
facial, due to pontine disease, 864.
facial or mimic spasm, 866.
facial hemiatrophy, 863.
glossopharyngeal, 870.
hypoglossal, 873.
of fifth (trigeminal) nerve, 862.
of fourth (trochlear) nerve, 861.
of ocular nerve, 860.
of olfactory nerve, 856.
of optic nerve, 857.
of seventh nerve (facial), 863.
of sixth (abducens) nerve, 861.
of spinal accessory nerve, 871.
of third nerve (motor oculi), 860.
ophthalmoplegia, 861.
pneumogastric, 871.
spasm of spinal accessory muscles, 872.
tic convulsive with, 867.
location of lesion causing, 856.
lumbosacral, 879.
sacral, 882.
Peripylephlebitis syphilitica, 702.
Periserositis, 662.
Perisigmoiditis, 642.
Perisplenic abscess, 1170.
Perisplenitis, 1170.
Peritoneum, diseases of, new growths of, 663.
peritonitis, acute diffuse, 659.
peritonitis, chronic, 662.
tuberculous. See Tuberculosis.
endothelial degeneration of, 663.
fatty deposits of, 663.
innocent cysts and echinococcus of, 663.
imitation of bacterial virulence and proliferation by, 660.
neoplasms of, 663.

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Peritoneum, secondary carcinomata of, 664.
Peritonitis, acute diffuse, with appendicitis, 659, 661.
early control of, 662.
kidney and liver in, 661.
temperature in, 661.
acute localized, 662.
associated conditions of, 659-660.
chronic, 662.
pus accumulation in, 662.
chronic nodular proliferative, 663.
deforming and obliterating, 662.
favorable cases of, 661.
general, 660.
hemorrhagic, 663.
hiccough with, 875.
idiopathic, 659.
in nephritis, 792.
localized and protective, 660.
origin of, 659.
perforative, gravity of, 660.
in typhoid fever, 104-105.
puerperal, 661.
rheumatic, 659.
suppurative, in pneumonia, 167.
tuberculous, 257.
with cirrhosis, 686.
with rheumatic fever, 289.
Peritonsillitis, acute suppurative, 297.
Perityphlitis, 644.
Pertussis. See Whooping-cough.
Pestis minor, 205.
Petit mal, 1046-1055.
Pfeiffer's disease, 353.
Pharyngitis, acute catarrhal, 559.
catarrhal, in typhoid fever, 97.
chronic, 560.
chronic alcoholic, 1181.
phlegmonous, 560.
ulcerative, 560.
Pharyngitis sicca, 560.
Pharynx, diseases of, circulatory anomalies, 559.
pharyngitis, 559.
edema of, 559.
hemorrhagic symptoms of, 559.
hyperemia of, 559.
Phlebitis, sinus, following otitis, 955.
septic, in appendicitis, 658.
Phlebitis cruralis, in typhoid fever, 95.
Phlegmons, in typhoid fever, 107.
Phobias, of neurasthenia, 1030.
Phosphates, triple, in urine, 778.
Phosphaturia, 777.
Phosphorus poisoning, differentiated from acute yellow atrophy of liver, 674.
Phrenic neuralgia, 843.
Phrenic paralysis, bilateral, 874.
causes of, 874.
prognosis of, 875.
Phthisis, See Pulmonary Tuberculosis.
fibroid, 244.
Physical agents, diseases due, to caisson disease, 1207.
mountain sickness, 1209.
sunstroke, 1205.
Pia mater and arachnoid, inflammation of, 937.
Pick's disease, 432, 702.
Pilocarpin, in sympathicotonia, 1083.
vagotonia due to, 1082.
von Pirquet's test, 239.
Pituitary gland, diseases of, hyperpituitarism, 1160.
hypopituitarism, 1158.
importance of, 1161.
Plague, bubonic, 203.
character of, 201.
complications in, 206.
general considerations of, 205.
history of, 202.
mode of entry of, 203.
pestis minor, 205.
pneumonic, 204.
septicemic, 204.
symptoms of, 205.
transmission of, 202.
Plethora, and obesity, 1127.
Plethora vera. See Erythremia.
Pleura, diseases of, hydrothorax, 396.
mediastinal, 399.
pleurisy, 389.
pneumothorax, 396.
Pleurisy, atelectasis in, 391.
chronic, fibroid pneumonia due to, 395.
nature of, 395.
serofibrinous cysts with, 395.
with multiple adhesions, 395.
with proliferative changes, 395.
differentiation of tuberculous and non-tuberculous, 392.
dry, 248, 389.
fibrinous, 389.
associated symptoms of, 389.
primary, 389.
secondary, 389.
hemorrhagic, 396.
in cirrhosis, 694.
in influenza, 127.
in pneumonia, 165.
in scarlet fever, 330.
interlobular, 391.
in typhoid fever, 98.
pneumococcus, 389-390.
purulent, 392.
associated symptoms of, 393.
general statements on, 393.
in typhoid fever, 99.
secondary, 392.
virulent types of, 393.
serofibrinous, 389.
associated symptoms of, 390.
double, 391.
general considerations on, 391.
mortality from, 392.
persistent dyspnea with, 391.
symptoms of, 390-391,
temperature in, 390.

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Pleurisy, serofibrinous, tuberculous. See Tuberculous pleurisy.
unfavorable, 391.
with diphtheria, 142.
with effusion, 389.
with endocarditis, 491.
with rheumatism, 288.
Pleuropneumonia. See Pneumococcus infection.
Plumbism. See Lead poisoning.
Pneumaturia, 787.
Pneumococcus infection, general, manifestations of, 146.
lobar pneumonia, 145.
pneumococcemia, 146.
Pneumococcus meningitis, 159.
Pneumogastric paralysis, associated conditions of, 871.
compression of nerve at base in, 871.
primary, 871.
Pneumonia, acute dilatation of stomach with, 577.
and tuberculosis, 163-164.
blood condition in, bacteremia, 156.
blood-plates, 158.
coagulation time, 158.
diminution of carbon dioxid, 156.
eosinophilia, 157.
increase of fibrin, 158.
leukocytosis, 156-157.
lymphocytes, 157.
myelocytes, 158.
urobilin, 158.
blood-pressure in, Gibson's rule, 148.
catarrhal, 169.
chronic non-tuberculous, fibrinous or catarrhal, 379.
general conclusions on prognosis of, 380-381.
interstitial, 379.
pneumonokonioses, 280.
tuberculosis developed from, 381.
circulation in, collapse, 154.
cyanosis, 153.
influence of toxemia on heart and vasomotors, 147-153.
irregularities of heart, 154.
previous disease of heart, 153-154.
complications in, arthritis, 167.
bronchitis, 165.
bronchorrhea, 165.
emphysema, 166.
empyema, 164-165.
endocarditis, 167.
fibrosis of lung, 166.
gangrene of lung, 164.
lung abscess, 165.
metastatic parotitis, 168.
neuritis, 168.
otitis media suppurativa, 167.
pericarditis, 166.
peritonitis, 167.
pleurisy, 165.
pulmonary edema, 164.
purpura, 167.
purulent infiltration of lung, 166.
Pneumonia, croupous, 146.
clinical varieties of, 162.
afebrile, 162.
alcoholic, 162.
aspiration, 163.
asthenic, 162.
bilious, 162.
embolic, 163.
hypostatic, 163.
influenzal, 163.
migratory, 163.
complications in, tuberculosis, 163-164.
pneumococcemia in, 146.
desquamating, 169.
due to occupation, 380-381.
empyema with, 393.
factors in prognosis of, age, 148.
alcoholism, 149.
association of diseases, 149.
blood pressure study, 147-148.
condition of life, 149.
effect of toxemia and associated lung lesion on cardiovascular system, 147.
extent of pulmonary and associated lesions, 150-151.
malignancy of infecting organism, 147.
predisposition to, 150.
pregnancy, 150.
race, 149.
resistance of patient, 148.
seasonal influences, 150.
sex, 150.
traumatism, 150.
fibroid, due to chronic pleurisy, 395.
fibrosis of lung in, 166.
gangrene due to, 385.
gastro-intestinal system in, dilatation of stomach, acute, 157, 161.
hiccough, 161.
membranous colitis, 161.
meteorism, 161.
vomiting, 161.
greater frequency of, among men, 150.
hemoptysis of, 376.
herpes labialis in, 161.
immunity following, 150.
in congenital syphilis, 67.
in diabetes mellitus, 1117.
influence of, on endocarditis, 485.
influence on, of prophylactic vaccination, 169.
in scarlet fever, 329.
insular, 169.
in tabes dorsalis, 58.
lobar, 145.
symptom complex of, 145.
lobular, 169.
membranous colitis in, 161.
meningococcus, in cerebrospinal meningitis, 184.
mortality from, among mental defectives, 150.
nervous system in, of alcoholics, 159.
convulsions, 159.

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Pneumonia, nervous system in, delirium, 159.
headaches, 159.
lumbar puncture, 159.
meningismus, 159.
pneumococcus meningitis, 159.
postpyrexial delirium, 160.
spinal fluid, 159.
toxemia of, 158.
physical signs of, 162.
post scarlatinal, 332.
respiratory system in, cough, 155.
frequency of respirations, 154-155.
severe pain in pleura, 154.
sputum, 155.
symptoms of, 154-155.
secondary, 169.
skin in, 161.
spleen in, 162.
statistics and results of treatment in, 168.
sweating in, 161.
temperature in, chill, 151.
fever, 151-152.
tuberculosis, 244.
urinary system in, albuminuria, 160.
chlorid excretion, 160.
nephritis, 160.
quantity of urine, 160.
sugar, 160.
urea and uric acid, 160.
with cerebral hemorrhage, 972.
with cirrhosis, 694.
with diphtheria, 142.
with epilepsy, 1056.
with influenza, 126-127.
with influenzal meningitis, 126-127.
with malaria, 77.
with pyemia, 133.
with rheumatism, 288.
with sepsis, 133.
Pneumonic plague, 204.
Pneumonic tuberculosis, 228.
chronic interstitial, 244, 245, 246.
Pneumonokonioses, 380.
Pneumopericardium, 434.
Pneumothorax, considerations in prognosis of, 397-398.
dangers of, 397.
due to empyema, 398.
general considerations on, 397.
in typhoid fever, 99.
in tuberculosis, 397.
statistics on, 397-398.
with pus (pyopneumothorax), 396.
with serum (hydropneumothorax), 396.
Poisoning, tetany due to, 1167.
Poisons, neuralgia due to, 839.
Polioencephalitis, 322, 975.
Polioencephalitis inferior, 976.
Polioencephalitis superior, of alcoholic origin, 975.
psychic disturbances with, 975.
respiratory paralysis with, 975.
Polioencephalomyelitis, 976.
Poliomyelitis, 854.
acute anterior, abortive type of, 320.
ataxic type of, 323.
bulbar and pontine types of, 322.
cerebral type of, 322.
conclusions on, 324.
electrical reactions in, 323.
general considerations of, 323.
Landry type of, 322.
lumbar puncture for, 323.
meningitic type of, 323.
mortality from, 324-325.
polyneuritic type of, 323.
prodromal period of, 319.
spinal, 321.
sporadic cases of, 324.
stage of paralysis in, 320.
chronic, 326.
encephalitic, 975.
Flexner's and Noguchi's findings on, 318.
"healthy carriers" of, 319.
increase in number of cases of, 318.
increase in severity of, 319.
nature of, 317.
pathologic area of, 318.
period of incubation of, 319.
port of entry of, 319.
"rudimentary," 320.
Pollantin, 359.
Polyarthritis, acute. See Rheumatic fever.
destructive chronic, arthritis deformans, 1088.
rheumatism, chronic articular, 1088.
non-suppurative, in scarlet fever, 332.
Polycystic kidney, leading symptoms of, 827.
nature of, 827.
Polycythemia, symptomatic. See Erythremia, secondary.
Polycythemia vera. See Erythremia, primary.
Polyneuritis, 848.
acute febrile, 853.
glucosuria in alcoholics with, 1118.
tuberculous, 278.
Polypi, of esophagus, 568.
Polypoid growths, 358.
of intestines, 644.
Polyplasma, 518.
Polyserositis, chronic, 432.
Polyuria, in chronic interstitial nephritis, 807.
in diabetes mellitus, 1114.
Pontine disease, facial paralysis due to, 864.
Popliteal nerve, external, paralysis of, 881.
internal, paralysis of, 881.
Portal pyemia, 678, 679, 707.
Portal vein, diseases of, pylephlebitis, 678.
thrombosis, 678.
Postbasic meningitis, 934.
Posterior disease, combined lateral and, 901.

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Posterior thoracic nerve, paralysis of, 877.
Postpyrexial delirium, 160.
Pregnancy, albuminuria of, 794.
and epilepsy, 1051.
and obesity, 1128.
and pneumonia, 150.
chorea due to, 1040.
in paratyphoid, 123.
in tuberculosis, 241-251.
in typhoid, 110.
myelitis of, 907.
nephritis of, 794.
nephritis aggravated by, 796.
Priapism, in leukocytic leukemia, 532.
Profeta law, 65.
Prognosis, Alpinus, Prosper, on, 4.
Chauffard on, 5.
collective investigation of disease in, 9.
definition of, 1.
Duckworth, Sir Dyce, on, 5.
endogenous influences in, 6, 7, 8, 9.
exogenous influences in, 6-7.
factors in, after effects of disease, 7-8.
age, 6.
constitution, 7.
diathesis, 7.
early diagnosis, 6.
general survey of patient, 11-12.
influence of acute infections, on existing chronic diseases, 8-9.
latency of symptoms, 11.
localization of lesions, 6.
neuropathic tendencies, 8.
occupation, 6.
phagocytosis, 8.
race, 7.
tolerance of organs to pathologic change, 6.
varying character of epidemics, 7.
giving of, to patient, 10-11.
Harvey, J., on, 4.
Hippocrates on, 2-3.
honest suggestion with, 11.
in acute infections, 7.
in bacterial disease, 8.
in contagious diseases, 7-8.
in epidemics, 7.
in infectious diseases, 8.
Munk on, 4.
optimism in, 10, 11.
Paget, Sir James, on, 8.
publications dealing with, 4-5.
requirements for, 9.
setting of time limit in, 11.
Progeria, in infantilism, 1159.
Protozoan infections, amebic dysentery, 78.
Leishmaniasis, 83.
malaria, 72.
relapsing fever, 82.
syphilis, 15.
trypanosomiasis, 81.
Pruritus, in diabetes mellitus, 1118.
Pseudo-angina, 456.
Pseudobulbar paralysis, causes of, 893.
course of, 893.
infantile, 893.
symptoms of, 893.
Pseudoleukemia. See Leukemia, lymphatic. See Hodgkin's disease.
transition of, to leukemia, 541.
Pseudomultiple sclerosis, 913.
Pseudotabetic gliosis, 917.
Pseudotabetic symptoms, in arsenical multiple neuritis, 852.
Psilosis, 626.
Psychalgia, 841.
akinesia algera, 1086.
Psychasthenia, 1030.
Psychic disturbances, in brain tumor, 993.
in chorea, 1040.
in pellagra, 1200.
Psychoneurosis. See Hysteria.
Psychoses, due to influenza, 129.
Ptomain poisoning, 1203.
enteritis due to, 620.
Ptyalism, 556.
Puerperal erysipelas, 174.
Puerperal multiple neuritis, 854.
Pulmonary abscess, associated with empyema, 393.
hemoptysis of, 378.
Pulmonary apoplexy, 378.
Pulmonary cancer, 387.
Pulmonary complications, in appendicitis, 658.
in gout, 1105.
Pulmonary congestion, active, 373.
edema, 375.
hypostatic, 374, 375.
passive, 374.
Pulmonary edema, 375.
in nephritis, 792.
in pneumonia, 164.
in typhoid fever, 99.
with epilepsy, 1056.
Pulmonary embolism, with chlorosis, 518.
Pulmonary emphysema, caused by chronic bronchitis, 365.
Pulmonary gangrene, due to infarct, 378.
hemoptysis of, 377.
in pulmonary carcinoma, 387.
primary infections of, pneumonia, 385.
thrombosis or embolism of branch of pulmonary artery, 386.
Pulmonary hemorrhage, hemoptysis, by aspiration to other parts of lungs, 378.
due to aortic aneurism, 377.
due to chronic bronchitis, 377.
due to gangrene, 377.
due to heart disease, 376-377.
due to hemophilia, 377.
due to hyperemia, 376.
due to malignant growths, 376.
due to malignant purpura, 377.
due to mitral stenosis, 376.
due to pneumonia, 376.
due to syphilitic ulceration of air passages, 377.

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Pulmonary hemorrhage, due to ulcerative disease of upper air passages, 376.
due to vicarious menstruations, 376.
due to whooping-cough and measles, 377.
in arteriosclerosis, 377.
in nephritis, chronic interstitial, 377.
into air cells, 378.
Pulmonary infarct, 378.
in typhoid fever, 98.
Pulmonary insufficiency, 504.
Pulmonary neoplasms, primary, 387.
secondary, 388.
Pulmonary obstruction, congested kidney due to, 813.
Pulmonary pernicious malaria, 750.
Pulmonary stenosis, and associated conditions, 436-437.
compensatory hypertrophy, 435.
nature of, 435.
Pulmonary tuberculosis, age as factor in, 238.
and laryngeal, 251.
calcification or fibroid change in, 227.
caseous, 229.
cavity formation in, 230.
chronic, 229.
diazo-reaction in, 234.
disappearance of, due to, raised resistance of patient, 218-227.
due to measles, 344.
factors in, 226.
gangrene due to, 386.
incipient cases of, 237.
limited expansion of thorax in, 233.
lobar or pneumonic, 228.
lobular pneumonic, 227.
misshapen or retracted thorax in, 233.
physical signs of, of advancing disease, 238.
in incipient cases, 237.
in last stage, 238.
rheumatoid form associated with, 234.
röntgenoscopy in, 239-240.
symptoms of, blood conditions, 235, 236, 237.
cough, 229-230.
diarrhea, 232.
digestive, 234.
dyspepsia, 228.
expectoration, 229-230.
fever, 227, 231, 232.
heart, 233.
hemoptysis, 227-231.
hoarseness, 234.
infiltration of lung tissue, without cough, 230.
liver and spleen, 234.
loss of weight, 233.
nervous, 235.
nummular expectoration, 230.
pain, 233.
shortness of breath, 230.
urinary, 234.
tuberculin tests for, 238-239.
Pulmonary tuberculosis, ulcerative, 229.
with chlorosis, 518.
with cirrhosis, 686.
with defect in intraventricular septum, 436.
with epilepsy, 1056.
with perforate foramen ovale, 436.
Pulmonary valve, defects of, 503.
Pulse, alternate, 449.
Pupillary phenomenon, hysterical, 1013.
in cerebral hemorrhage, 965.
Purpura, chronic, alternation of, with erythema multiforme, 546.
blood picture of, 547.
continuous, 546.
intermittent, 546.
mode of termination of, 547.
nature of, 546.
rebellion of, to treatment, 546.
due to iodin, 543.
Henoch's, 547.
in congenital syphilis, 67.
in nephritis, 809.
in rheumatism, 290.
malignant, hemoptysis of, 377.
primary, chronic, 546.
hemophilia, 548.
Henoch's, 547.
purpura hemorrhagica, 545.
purpura rheumatica, 544.
purpura simplex, 543.
secondary, associated conditions of, 542.
prognostic import of, 543.
symptom complex of, 542.
Purpura fulminans, of adults, 545.
of infants, 544.
Purpura hemorrhagica, 545.
blood picture of, 545.
hemorrhage into appendix in, 545.
in typhoid fever, 106.
Purpura rheumatica, 544.
chorea with, 1039.
resemblance of, to erythema nodosum, 544.
Purpura simplex, 543.
Purpuric appendicitis, 649.
Pus casts, 750.
Pyelitis, acute, 831.
ascending, 832.
blood examinations in, 832.
calculous, 824, 831.
catarrhal, 830.
recurrence of, 831.
chemical and bacteriological examinations in, 832.
chronic, 831.
chronic cystitis with, 831.
cystoscopic examinations in, 832.
danger of neglected, 831.
definition of, 829.
distinguished from renal tuberculosis, 268.
gonorrheal, 832.
in enfeebled subjects, 830.
in typhoid, 110.

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Pyelitis, lack of bacteriological cure of, 832.
non-calculous, with hematuria, 759.
prognosis of, after local treatment, 833.
after operation, 831.
prognostic factors of, 830.
pyelography for, 832.
repeated chills and fever in, 834.
surgical treatment for, 831.
urine in, 833.
with tuberculosis of genito-urinary tract, 830.
x-ray in, 832.
Pyelocystitis, infection of, 830.
toxic symptoms of, 830.
Pyelography, in pyelitis, 832.
Pyelonephritis, acute, nephrotomy for, 831.
definition of, 829.
nephrectomy for, 831.
Pyemia, 131-132.
and pneumonia, 133.
due to aural and brain abscess, 984.
in actinomycosis, 301.
Pyemic infections, mixed with septic, 131.
Pylephlebitis, 678.
suppurative, 679, 704, 707.
Pylethrombosis, 678.
in amebic dysentery, 80.
Pyloric spasm, 581.
causes of, 582.
in hypermotility, 617.
Pyloric stenosis, benign acquired, acute inflammatory, 583.
chronic cicatricial, 583.
complete, 585.
dependent on active ulcer, 583.
dependent on non-malignant growths, 584.
due to distortion or traction, 584.
fibrotic, 583.
general fibrotic, 583.
hypertrophic, of Cruveilhier, 583.
localized fibrotic, 583.
syphilitic, 583.
tuberculous, 584.
benign functional, 581.
benign organic, 582.
acquired, 583.
congenital, 582.
extrapyloric, 584.
Pylorus, adhesions of, in cholelithiasis, 729.
Pyonephrosis, 815.
definition of, 829.
Pyopneumothorax, 396.
Pyothorax, 392.
Pyrexia, post-typhoid, 93.

Q

Quadriplegia, 846.
due to alcoholic multiple neuritis, 849.
Quincke's disease. See Angioneurotic edema.
Quinsy. See Peritonsillitis.

R

Rabies. See Hydrophobia.
Rachitis, acute, 1131.
advanced, 1129.
bony changes in, 1129.
causes of, 1129.
course of, 1129.
deformities of, 1130.
due to congenital syphilis, 67.
due to hereditary syphilis, 1129.
due to patent foods, 1129.
enlarged spleen and liver in, 1130.
excessive sweating of head in, 1130.
faulty diet in, 1130.
Harrison's sulcus in, 1130.
heredity in, 1129.
Hutchinson teeth in, 1130.
in poorer classes, 1129.
late, 1129.
persistent improper respiration in, 1130.
predisposition to, 1129.
"rosary" in, 1130.
severe cases of, 1130.
severity of infections in, 1130.
tardiness of walking in, 1130.
tendency to recovery in, 1130.
Radial paralysis, 878.
Railroad spine. See Traumatic neurosis.
Ray fungus, 301.
Raynaud's disease, age in, 1070.
and erythromelalgia, 1067.
characteristic symptoms of, 1069.
complications in, 1072-1073.
family predisposition to, 1070.
first stage of, local syncope, 1070.
frequency of, 1070.
gangrenes not included in, 1070.
prognosis for life in, 1074.
seasonal influences in, 1070.
second stage of, local asphyxia or cyanosis, 1071.
sex influence in, 1070.
third stage of, symmetrical gangrene, 1072.
thyroid treatment for, 1073.
Reaction of degeneration, in facial paralysis, 865.
in idiopathic multiple neuritis, 854.
in lead multiple neuritis, 851.
in peripheral neuritis, 847.
Reactions, electrical, in poliomyelitis, 323.
von Recklinghausen's disease, 883.
Rectum, syphilis of, 34.
Reflex excitability, hysterical, 1015.
Refraction, errors of, 857.
Reichman's disease, 618.
suggestive of ulcer, 589.
Relapsing fever, 82.
Relapsing typhus. See Relapsing fever.
Renal asthma, 370.
and nephritis, 370.
Renal calculi, cystin stones, 821.
hematuria due to, 759.
large, 821.
multiple, 821.

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Renal calculi, sand or gravel, 821.
single, without infection, 821.
varieties of, 821.
xanthin stones, 821.
x-ray examination in, 821.
Renal cirrhosis, 804.
Renal colic, in nephrolithiasis, 823.
Renal epistaxis, indicated by hematuria, 757.
Renal function, estimation of, 770.
Renal growths, 825.
Renal infarct, hematuria with, and septic fever, 758.
Renal insufficiency, in chronic interstitial nephritis, 806.
in cirrhosis, 694.
Renal sclerosis, 804.
Renal sufficiency test, early application of, 773.
diagnostic and prognostic value of, 768.
for chronic nephritis, 800.
for estimation of incoagulable or non-protein nitrogen of blood, 771.
phenolsulphonephthalein, of Rowntree and Geraghty, 770.
of Thayer and Snowden, 772.
results of, 773.
Schlayer's, 769-770.
ureteral catheterization with, 773.
Renal system, diseases of, nephropathies, amyloid kidney, 814.
congested kidney, 811.
nephritis, acute parenchymatous, 788.
nephritis, chronic interstitial, 804.
nephritis, chronic parenchymatous, 797.
tuberculous kidney. See Tuberculous kidney.
suppurative, perinephric abscess, 834.
pyelitis, 829.
surgical, hydronephrosis, 815.
movable kidney, 828.
neoplasm, 825.
nephrolithiasis, 820.
Renal tuberculosis, bladder invasion in, 269.
blood pressure in, 270.
distinguished from pyelitis, 268.
early hematuria in, 269.
extent of, 269.
factors influencing prognosis of, 268.
perinephric abscess with, 269.
pregnancy and childbirth with, 270.
reduced functional activity in, 268.
surgical removal of primary focus in, 269.
with advanced pulmonary, 269-270.
with miliary infection, 268.
Respiratory symptoms, in exophthalmic goiter, 1146.
in typhoid fever, 96.
Respiratory system, actinomycosis of, 302.
anthrax, 211.
diseases of, bronchial, asthma, 368.
bronchiectasis, 366.
bronchitis, acute, 363.
bronchitis, chronic, 365.
bronchitis fibrinous, 373.
syphilis, 33.
whooping-cough. See Pertussis.
laryngeal, edema, 362.
laryngismus stridulus, 362.
laryngitis, acute, 360.
laryngitis, chronic, 361.
laryngitis, syphilitic. See Syphilitic laryngitis.
laryngitis, tuberculous. See Tuberculous laryngitis.
syphilis, 33.
nasal, acute catarrhal rhinitis, 357.
epistaxis, 359.
hay fever, 358.
nasal, 32.
pleural, hydrothorax, 396.
mediastinal, 399.
pleurisy, 389.
pneumothorax, 396.
pulmonary, abscess, 386.
congestion, 373.
emphysema, 382.
gangrene, 385.
hemorrhage, 376.
neoplasm, 387.
non-tuberculous pneumonia, 379.
syphilis, 33.
effect on, of trichinosis, 313-314.
in alcoholism, 1183.
influence of, on endocarditis, 489.
in measles, 344.
in pneumonia, 154.
in scarlet fever, 329.
Retina, lesions of, causing blindness, 857.
in chronic nephritis, 803.
Retinal hemorrhages, with pernicious anemia, 527.
Retinitis, albuminuric, in chronic interstitial nephritis, 809.
Retrobulbar disease, 858.
Retropharyngeal abscess, 560.
Rheumatic fever, bacteriology of, 279.
complications in, appendicitis, 289.
blood, 287.
brain and nervous system, 287.
heart, bradycardia, 286.
endocarditis, 283.
myocarditis, 285.
pericarditis, 285.
tachycardia, 286.
hyperpyrexia, 286.
kidney, 288.
lung and pleura, 288.
peritonitis, 289.
purpura, 290.
rheumatic nodules, 289.
septic, 289.
skin, 289.
duration of, 290.
factors influencing prognosis of, 279.
age, 281.
character of onset, 281.

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Rheumatic fever, factors influencing prognosis of, coincident disease, 282.
environment and social conditions, 291.
preëxisting diseases, 281.
resistance of patient, 280.
sex, 280.
immunity to, 291.
mortality from, 279.
nature of, 278.
number of joints inflamed in, 290.
recurring, 290.
relapses of, 291.
symptoms of onset of, 281.
Rheumatic nodules, 289.
Rheumatism, chorea and endocarditis with, 284.
chronic articular, pathological similarity of, to arthritis deformans, 1088.
gonorrheal, 192.
inflammatory. See Rheumatic fever.
muscular. See Myalgia.
pleurisy and, 288.
Rhinitis, acute catarrhal, extension of, 357.
primary, 357.
secondary, 357.
syphilitic, 357-358.
Rhinologic abscess of brain, 985.
Rickets. See Rachitis.
Romberg symptoms, of tabes dorsalis, 55.
Röntgenoscopy, for tuberculosis, 239-240.
Rose cold. See Hay fever.
Roseola, epidemic, 346.
in typhoid fever, 106.
See Measles.
Rothera test, for acetone, Garrod's modification of, 1115.
Round worms, 315.
Rubeola, 346.
Rubeola scarlatinosa, 352.
Rupture of esophagus, 568.
Rupture of heart, 466.
Rupture of valves, 500.

S

Sachs' disease. See Idiocy, amaurotic family.
Sacral plexus, paralysis of, 882.
Salivary glands, diseases of, Mikulicz's disease, 557.
mumps. See Parotitis, epidemic.
parotitis, 557.
Salivary swellings, bilateral, 557.
Salvarsan, encephalitis due to, 976.
in pernicious anemia, 528.
polyneuritis due to, 852.
Sarcoma, of brain, 996.
of intestines, 644.
of kidney, 825.
of liver, 709-711.
of spinal cord, 923.
infiltration in, 924.
Sarcoma, of spinal cord, multiple, 924.
Saturnine anemia, 1190.
Saturnine arteriosclerosis, 1192.
Saturnine arthralgia, 1189.
Saturnine nephropathy, 1192.
Scanning speech, in multiple sclerosis of brain and cord, 910.
Scarlatinoid, 352.
Scarlet fever, albuminuria with, 746.
and measles, 345.
character of, 327.
classification for prognosis, 332.
complications in, adenitis, 332.
arthritis, 332.
endocarditis, 330.
myocardial degeneration, 330.
nephritis, 331.
nephritis, with endocarditis, 330.
respiratory, 329.
uremic poisoning, 331.
mild, 328.
pleurisy in, 330.
prognosis of, 328-329.
symptoms of, blood, 330.
cardiovascular, 330.
diphtheritic, 329.
ear, 329.
general, 328-329.
increasing anemia with eye symptoms, 332.
pulse, 330.
renal, 331.
without rash and with slight tonsillitis, 328.
Schmidt's bile test, in summer diarrhea of infants, 629.
Schoenlein's disease, 544.
Sciatic neuralgia, 844.
Sciatic pain, with tumors of spinal cord, 921.
Sciatic paralysis, 880-881.
Sciatica, 844.
Sclerodactylia, 1077.
Scleroderma, acute, 1077.
causes of, 1077.
circumscribed, 1077.
definition and nature of, 1077.
duration of, 1077.
heredity in, 1077.
intercurrent disease in, 1078.
joint changes in, 1077.
pigment deposit and bronzing in, 1077.
prognosis of, 1078.
recession of lesions in, 1077.
typical cases of, 1077.
Sclerosis, amyotrophic lateral, 890.
congenital lateral, cause of, 900.
diplegic character of, 901.
prognosis of, 901.
symptoms of, 900.
coronary, 454.
disseminated nodular. See Multiple sclerosis of brain and cord.
disseminated, of optic nerve, 858.

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Sclerosis, multiple, of brain and cord. See Multiple sclerosis of brain and cord.
primary lateral, advanced, symptoms of, 900.
character of, 899.
course of, first stage, 899.
second stage, 900.
terminal or third stage, 900.
stationary periods of, 900.
weakness of legs in, 900.
pseudomultiple, 913.
Sclerosis en placque. See Multiple sclerosis of brain and cord.
Scorbutus, adult, causes of, 1132.
endemic, 1133.
malignant, 1133.
origin and association of, 1132.
symptoms and infections of, 1133.
infantile, causes of, 1133.
symptoms of, 1133.
Scrivener's palsy, 1064.
Scrofula, 265.
Scurvy. See Scorbutus.
Secretory disturbances, hysterical, 1018.
Senile heart, 460.
Senile kidney, 805.
Sensory disturbances, in chorea, 1041.
in neurasthenia, 1030.
Sepsis, 130, 131, 132, 133.
duration of, 133.
in rheumatism, 289.
Septic meningitis, 133.
Septic thrombosis, 132.
Septicemia, character of, 130-131.
Septicemic plague, 204.
Septicopyemia, 130.
Serratus magnus, paralysis of, 877.
Seventh nerve, paralysis of, 863.
Sexual anomalies, hysterical, 1018.
in diabetes mellitus, 1117.
Sexual hypochondriacs, 1028.
Sexual neurasthenia, 1028-1029.
Shaking palsy. See Paralysis agitans.
Shingles. See Herpes zoster.
Ship fever. See Typhus fever.
Siderosis, 380.
Silicosis, 380.
Sinus phlebitis, following otitis, 955.
Sixth nerve, paralysis of, 861.
Skin, actinomycosis of, 302.
in paratyphoid, 123.
in typhoid fever, 106.
Skin changes, in arsenical poisoning, 1194.
in diabetes mellitus, 1118.
in exophthalmic goiter, 1147.
in gout, 1104.
in measles, 343.
in pellagra, 1200.
Skin diphtheria, 138.
Sleeping sickness. See Trypanosomiasis.
Smallpox, age in, 334.
black, 337.
classification of, 335.
variola without eruption, 337.
variola hemorrhagica, 337.
Smallpox, classification of, variola vera, 336.
varioloid, 337.
complications in, 338.
confluent, 337.
discrete, 336.
epidemics of, 334.
general considerations on, 333.
general statement on, 336.
hemorrhagic, 337.
historical data for, 333.
immunity to, 334.
nature of, 333.
pustular hemorrhagic, 336.
race in, 334.
sex in, 334.
stage of eruption of, 335.
stage of incubation of, 334.
stage of invasion of, 334.
symptoms of, backache, 334.
blood, 336.
cerebral invasion, 334.
enlarged spleen, 335.
eruptions, 335.
pulse, 335.
pustulation, 335.
temperature, 336.
vaccination against, 333.
influence of, on prognosis, 340.
rules for, 339-340.
Smell, hysterical perversion of, 1011.
loss of, 856.
perversion of, 857.
Spasm, facial, 866.
hysterical, 1014.
in brain tumor, 994.
in exophthalmic goiter, 1144.
mimic, 866.
muscular, in myotonia, 1085.
of sternocleidomastoid, 872.
of trapezius, 872.
Spasm of diaphragm. See Hiccough.
Spastic paralysis, 899.
family type of, associated with idiocy, 903.
with hydrocephalus, 945.
Spastic paraplegia. See Sclerosis, primary lateral.
secondary, 902.
Spinal accessory, neuritis, 872.
paralysis, causes of, 871-872.
Spinal anemia, complete, 928.
due to arterial obstruction, 927.
effect of, on primary disease, 928.
local, 927.
prognosis of, 928.
secondary, 927.
symptoms of, 928.
Spinal arteriosclerosis, 929.
Spinal congestion, passive, 928.
Spinal cord, abscess of. See Abscess of Spinal Cord.
affections of blood vessels of, 927.
anemia of. See Spinal anemia.
carcinoma of, 924.
changes in arteries of, 928.

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Spinal cord, gliosis of, 914.
hyperemia of, 928.
sarcoma of. See Sarcoma of Spinal Cord, 923.
tubercle of, 924.
tumors of. See Tumors of Spinal Cord.
Spinal cord diseases, afferent or sensory system, general paralysis of insane. See Paresis.
hereditary ataxia, 887.
herpes zoster, 885.
Marie's hereditary ataxia, 888.
tabes dorsalis. See Tabes dorsalis.
taboparesis. See Taboparesis.
anterior of efferent or motor tract. Landry's ascending paralysis. See Landry's Paralysis, 888.
muscular dystrophies, 895.
myotonia congenita, 898.
poliomyelitis anterior, 854.
progressive central muscular atrophy, 888.
progressive neural muscular atrophy, 894.
indiscriminate, abscess, 914.
of blood vessels, 927.
caisson disease. See Caisson disease.
multiple sclerosis of brain and cord, 908.
myelitis, 904.
pseudomultiple sclerosis, 913.
syringomyelia, 914.
tumors, 918.
lateral, amyotrophic lateral sclerosis. See Amyotrophic lateral sclerosis.
ataxic paraplegia, 901.
congenital lateral sclerosis, 900.
Erb's syphilitic spinal paralysis. See Syphilis of cord.
idiocy, amaurotic family, 903.
paraplegia, secondary spastic, 902.
primary lateral sclerosis, 899.
Spinal embolism, 929.
Spinal endarteritis, 929.
Spinal fever, sporadic, 934.
Spinal fluid, in epidemic cerebrospinal meningitis, 182-183.
Spinal hematoma, 931.
Spinal hemorrhage, causes of, 930.
prognosis of, 931.
spontaneous, 930.
symptoms following, 930.
traumatic cases of, 931.
Spinal leptomeningitis, acute, 933.
chronic, 933.
Spinal membranes, diseases of, hematoma, 931.
hemorrhage, 930.
spinal meningitis, 931.
most frequent forms of, 931.
Spinal neurasthenia, 1028.
Spinal pachymeningitis, definition of, 932.
external, diseases primary to, 932.
following surgical operations, 932.
lumbar fluid in, 932.
Spinal pachymeningitis, external, prognosis of, 932.
internal, 932.
Spinal paralysis, due to syphilis, 36.
Spinal syphilis, 35.
effects of, 36.
Erb's syphilitic spinal paralysis, 37.
paralysis due to, 36.
reactions in, 36.
relapse of, 37.
symptoms of, 35-36.
without cord involvement, 36.
Spinal thrombosis, 929.
Spinal vessels, advanced change in, 929.
Spine, concussion of, 1021-1022.
railroad, 1021.
typhoid, 112.
Spleen, abscess of, 80, 1170.
amyloid degeneration of, 34, 1170.
changes in, due to malaria, 73, 74, 77.
condition of, in leukemia, 531-532.
cyst of, 1171.
diseases of, mobile spleen, 1173.
splenomegaly, primary, 1171.
splenomegaly, secondary, 1169.
enlargement of. See Splenomegaly.
gummata of, 33.
hydatid cysts in, 308.
in erythremia, 550.
infarct of, 1171.
influence of, on hemolytic jaundice, 668.
in lymphatic leukemia, 533.
in pneumonia, 162.
in typhoid fever, 107.
mobile, 1173.
perforation of, 1170.
rupture of, 1171.
syphilis of, 33, 1170.
tuberculous, 262, 1170.
Splenectomy, in cirrhosis of liver, 682.
in leukemia, 535.
in pernicious anemia, 523.
Splenic abscess, in amebic dysentery, 80.
Splenic anemia, characteristic symptoms of, 1172.
in children, 1173.
prognosis of, 1173.
Splenic anthrax, 211.
Splenomegaly, of Gaucher type, 1171.
primary, 1171.
secondary, abscess with, 1170.
acute, 1169.
amyloid, 1170.
chronic, 1169.
with polycythemia, 1170.
cyst with, 1171.
infarct with, 1171.
in otherwise healthy subjects, 1170.
in syphilis, 34.
passive congestion with, 1170.
perforation in, 1170.
perisplenic abscess in, 1170.
perisplenitis or capsulitis with, 1170.
prognostic factors in, 1170.
rupture in, 1171.
syphilitic, 1170.

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Splenomegaly, secondary, tuberculous, 1170.
with liver cirrhosis, 1171.
splenic anemia in, 1172.
Spondylitis. See Marie's disease.
Sporadic spinal fever, 934.
Spotted fever. See Typhus fever.
Sprue, 626.
St. Vitus' dance. See Chorea.
Staggering, cerebellar, 1003.
Staphylococcus infection, 131.
Stasis, in chronic interstitial nephritis, 807.
Status epilepticus, 1054.
Status thymo-lymphaticus, 363, 370, 1164.
Stegomyia fasciata, 347.
Stenosis, extrapyloric, 584.
intra-esophageal, 566.
intrapyloric, 583.
tricuspid, 503.
Stenosis of aortic orifice, 438.
Stenosis of glottis, in syphilis, 33.
Stenosis of mitral and tricuspid valves, 439.
Stenosis of pulmonary orifice, 435.
Sternomastoid, paralysis of, 872.
spasm of, 872.
Stern's basedowoid disease, 1149.
Still's disease, 1092.
Stokes-Adams' disease, associated conditions of, 463.
deaths due to, 464.
duration of, 464.
mercury and neosalvarsan, treatment of, 464.
phenomena of, 463.
prognosis of, 464.
Stomach, catarrh of, 570.
chronic catarrh of, 572.
cirrhosis of, 572.
diseases of, cancer, 600.
dilatation, 576.
enteroptosis, 579.
gastritis, 570.
gastroptosis, 579.
gastrorrhagia, 613.
hematemesis, 613.
pyloric obstruction, 581.
syphilis of, 34.
tuberculosis of, 253.
Stomach contents, examination of, in gastritis, 574.
in early diagnosis of cancer, 602.
in gastric ulcer, 589.
Stomach lesions, in cirrhosis, 685.
Stomachal vertigo in chronic gastritis, 575.
in dilatation of stomach, 578.
Stomatitis, aphthous, 553.
aphthous, epidemic. See Foot and Mouth Disease.
causative relations of, 555.
causes of, 553.
erythematous, 553.
extent of inflammation in, 553.
gangrenous, 555.
Stomatitis, herpetiform, 554.
mercurial, 556.
simple catarrhal, 553.
ulcerative, in cancer of stomach, 607.
in measles, 344.
primary, 554.
secondary, 554.
symptoms of, 554.
Stomatitis neurotica chronica, 554.
Stomatitis parasitica, 556.
Strangulated intestines, due to false ligaments, 636.
due to hernia, 637.
due to incarceration through slits and apertures, 637.
due to isolated bands and adhesions, 637.
due to Meckel's diverticulum, 636.
due to normal structures abnormally attached, 637.
due to omental cords, 636.
Streptococcus erysipelatis, 173.
Streptococcus infection, 131, 132, 133.
Streptococcus tonsillitis, 293.
Streptococcus viridans infection, with chorea, 1039.
Streptothrix, 301.
Stricture. See Stenosis.
Subphrenic abscess, in cholelithiasis, 730.
Subscapular paralysis, 877.
Substernal struma, 1164.
Sunstroke, atmospheric influence in, 1206.
contributing factors to, 1205.
dangers of, immediate, 1205.
remote, 1206.
effects of, asthenia and myasthenia, 1206.
changed disposition, 1206.
epilepsy, 1051, 1206.
meningitis, 1206.
mental lethargy and loss of memory, 1206.
ocular disturbances and deafness, 1206.
psychoses, 1206.
tendency to recurrence of hyperpyrexia, 1206.
mortality from, 1206.
occurrence of, 1205.
symptoms of, deep coma, 1206.
delirium, 1206.
focal, 1206.
hemiplegia, 1206.
hyperpyrexia, 1205.
in obese patients, 1206.
irregular respiration, 1205.
meningitis and encephalitis, 1206.
paralysis, 1206.
sudden vertigo, 1205.
thermic fever due to, 1206.
Supraclavicular paralysis, 876.
Supra-orbital neuralgia, 841.
Suprarenal gland, diseases of, Addison's. See Tuberculosis of Suprarenal Bodies.
Suprarenal tuberculosis, chronic, 264.
duration of, 264.

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Suprarenal tuberculosis, chronic, symptoms of, 263.
syphilitic deposit in, 264.
Swallowing, difficult, 870.
Sweating, in exophthalmic goiter, 1146.
Sweating sickness, 351.
Sydenham's chorea, 1037.
Sympathetic nervous system, diseases of, irritation of cervical sympathetic, 1082.
paralysis of cervical sympathetic, 1081.
vagotonia, 1082.
influence of, 1081.
Sympathicotonia, 1083.
Syphilis, 15.
acquired, 16.
alopecia in, 19.
aortitis syphilitica due to, 27.
arteritis and, 19, 26.
blood changes during early stages of, 17.
blood changes during tertiary stage of, 24.
cardiovascular lesions due to aortitis syphilitica, 27.
cardiovascular lesions due to arteritis, 26.
cardiovascular lesions due to endarteritis, specific obliterating, 27.
heart syphilis, 28.
latent, 29.
myocarditis, 29.
cerebrospinal fluid in, second stage of, 22.
during tertiary stage of, 24.
condylomata in, 19.
constitutional symptoms in, 18.
ear changes in, 20.
endarteritis, specific obliterating in, 27.
eye affections in, 20.
fever in, 19.
galloping, 20.
gummata in, 23.
gummata of nose in, 23.
gummata of scalp in, 23.
gummata of tongue, tonsils, soft palate and buccal mucosa in, 24.
Jarish-Herxheimer reaction, 21.
joint invasion in, 20.
leukocytosis in, 24.
lues maligna in, 20.
complicated with visceral lesions, 20.
lues maligna of liver in, 30.
lymphocytosis in, 24.
manifestations of, early, 16-22.
late, 23.
myocarditis, early, in, 19.
nephritis in, 19, 31.
of digestive tract, 34.
of liver, 30.
of nervous system, 35.
of respiratory organs, 33.
of spleen, 33.
Syphilis, acquired, optic, 43.
period of latency in, second stage of, 21.
phlebitis syphilitica in, 29.
previous disease in, 17.
primary stage of, 16.
"saddle-nose" in, 23.
secondary stage of, 18.
length of, 22.
skin lesions of, gummatous syphilids, 23.
in tertiary stage of, 23.
lues maligna, 20.
mucous patches, 18.
papular and pustular eruptions, 18.
papular syphilids, 23.
pustulation, early, 18.
roseola eruption, 18.
rupia syphilitica, 20.
in secondary stage of, 18.
squamous syphilids, 18.
ulceration, 20.
specific amyloid degeneration in, 27.
tabes dorsalis due to, 45.
tertiary stage of, 23.
metasyphilitic manifestations of, 44.
Neisser's statistics on, 25.
visceral syphilis in, 25.
tertiary lesions, frequency of, 24-25.
visceral, in tertiary stage, 25.
Wassermann reaction in, during primary stage, 18.
alcoholism in, 41.
and life insurance, 68.
and marriage, 68.
aneurysm due to, 421.
angina pectoris due to, 456.
aortic insufficiency due to, 500.
arteriosclerosis due to, 67, 404, 405.
arteritis due to, 26.
bronchial, 33.
cardiovascular, 26.
cerebral, 38.
cerebral hemorrhage due to, 960-961.
cerebrospinal, hereditary, 37.
classification for prognosis of, 15-16.
congenital, anemia of, 66.
arteriosclerosis in, 67.
arteritis due to, 67.
bone changes in, 67.
changes in nails and skin in, 66.
characteristic manifestations of, 66-67.
Colles-Baume law for, 65.
destructive disease of skin, nose and soft palate in, 67.
early pemphigus syphiliticus, 66.
effect of, on growth of child, 66.
on mental progress, 66.
on nervous system, 67.
enlargement of lymphatics in, 66.
eye lesions in, 67.
Hutchinsonian teeth in, 67.
hydrocephalus, 67.
intestinal lesions with, 67.

Digitized by Google

Syphilis, congenital, juvenile paresis due to, 65.
juvenile tabes dorsalis due to, 45-47.
latent, 65.
maternal transmission of, 65.
non-transmission of, to child, 66.
of liver, 30.
of spleen, 34.
pneumonia with, 67.
Profeta law for, 65.
purpura, 67.
rachitis due to, 67, 1129.
transmission of, to third generation, 68.
conjugal nervous lesions due to, 69.
edema of glottis in, 33.
epilepsy due to, 42, 1050.
Herxheimer reaction, in edema of glottis, 33.
immunity of affected child to, 66.
immunity of mother of syphilitic child to, 65.
in tuberculosis, 242.
laryngeal, 33.
manifestations of, early, 1622.
metasyphilis, 44.
paresis, 62.
tabes dorsalis, 45.
taboparesis, 61.
mortality among offspring of, 69.
myocarditis due to, 29.
nasal, 32.
neuralgia due to, 839.
of bones and joints, 32.
of cord and brain, 44.
of digestive tract, 34.
of esophagus, 34.
of intestines, 34.
of kidney, 31.
gummatous deposit in, 31.
of liver, acquired, 30.
acquired, jaundice, 30.
atrophy acute, 30.
cirrhosis complicated by, 31.
congenital, 30.
gummata, 30.
lues hereditaria tarda, 31.
lues maligna, 30.
specific treatment in, 31.
of muscles, 32.
of nervous system, 35.
of respiratory organs, 33.
of spleen, 33, 1170.
of stomach, 34.
of testicle, 32.
paresis as lesion of, 35.
paresis due to, 62.
pulmonary, 33.
rectal, 34.
shortening of life in, 68.
spinal, 35.
spinal leptomeningitis due to, 934.
stenosis of glottis in, 33.
tabes as lesion of, 35.
tertiary, Neisser's statistics on, 25.
tracheal, 33.
Syphilis, traumatic neurosis associated with, 1024.
Wassermann reaction in, negative, 19-21.
positive, 15, 18, 21, 22, 28.
Syphilitic anemia, 524.
Syphilitic aortitis, aneurism due to, 423.
Syphilitic brain tumor, 993.
Syphilitic cirrhosis, 701.
Syphilitic coryza, 358.
Syphilitic endocarditis, 504.
Syphilitic epilepsy, 42.
Syphilitic granuloma, 541.
Syphilitic hydrocephalus, 944, 945.
Syphilitic jaundice, 670, 671, 674.
Syphilitic myelitis, 906.
Syphilitic nephritis, 790.
Syphilitic peripheral neuritis, 37.
Syphiiltic pyloric stenosis, 583.
Syphilitics, fate of, 69.
offspring of, 69.
Syphilomata, of brain, 997.
Syringomyelia, classification of, 915.
congenital, 914-915.
diabetes mellitus with, 917.
direct causes of death from, 918.
due to pressure from tumors, 915.
due to traumatism, 914.
duration of, 918.
futility of treatment for, 917-918.
muscular atrophy in, 915.
spinal curvature in, 917.
symptoms of, 914.
bulbar, 917.
muscular atrophy, 915.
psychic, 917.
sensory disturbances, 915-916.
trophic, 916.
tabes dorsalis and paresis with, 917.
tabes of spine with, 917.
with acromegaly, 918.
with pachymeningitis, cervical hypertrophic, 917.
Syringomyelic symptoms, in hematomyelia, 930.

T

Tabes, arsenical, 1193.
Tabes dorsalis, 45.
as syphilitic lesion, 35.
blood and fluid during initial stage of, 50.
causes of, 46.
causes of death in, 58, 59, 60.
causes of rapid progression of, 56.
complications in, alcoholism, 58.
aortitis, 58.
arteriosclerosis, 58.
arteritis, 58.
Basedow's disease, 58.
epileptiform seizures, 59.
hemorrhagic conditions, 60.
hysteria, 59.
infections, 58.
invasion of medulla oblongata, 58.

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Tabes dorsalis, complications in, paralysis agitans, 58.
pneumonia, 58.
septic conditions, 59.
surgical operations, 58.
trauma, 58.
tuberculosis, 58.
vertigo, 59.
duration of, 60.
effect of trauma in, 58.
general conclusions on, 60.
influence of treatment, on various stages, ataxic, 52.
incipient, 48-51.
paralytic, 52.
juvenile, 45-47.
manifestations of, 45-46.
morphin habit in, 54.
ophthalmoplegia in, 56.
pneumonia in, 58.
predisposing factors to, age, 47.
complications, 58.
location and extent of degeneration, 48.
prognostic significance of separate symptoms, 53-57.
prophylaxis, 47-48.
sex, 47.
social status, 58.
treatment, influence of, on various stages of disease, 48-53.
prevention of, in syphilis, 39.
prognosis of life of patient in, 60-61.
prognostic conclusions, of initial stage, 51.
psychic element in, 56-59.
single symptom, without progression, 49.
social status of patient in, 59.
stages of, ataxic, 52.
initial or neuralgic, 48-51.
paralytic, 52.
stationary, 49-50.
symptoms of, Argyll-Robertson pupil, 56.
arthropathies, 57.
ataxia, 55.
ataxic stage, 52.
atrophy of optic nerve, 54.
bladder, 55.
gastric crises, 49-53.
hypotonia, 56.
impotence, 56.
initial stage, 49-51.
multiplicity of, 53.
ocular paralysis, 56.
ophthalmoplegia, 56.
paralytic stage, 52.
perforating ulcer, 57.
prognostic significance of, 53.
rectal, 55.
Romberg, 55.
Westphal, 55.
treatment of, Donath's conclusions on, 52-53.
Dreyfus report on, 52.
Tabes dorsalis, treatment of, Wassermann reaction in, 57.
with syringomyelia, 917.
Tabes inversa, 55.
Tabes mesenterica, 266.
of childhood, 266.
Taboparesis, 61.
Tachycardia, hysterical, 1019.
in diphtheria, 140.
in nephritis, 807.
paroxysmal, duration of, 509.
fluoroscope in, 509.
heart rate of, 509.
in women, 509.
symptoms of, 509.
simple, 510.
causes of, 510.
physiological, 510.
Tapeworm. See Cestodes.
Taste, hysterical perversion of, 1011.
loss of, 870.
perverted, 870.
Tenia echinococcus, 306.
mediocanellata, 305.
saginata, 305.
solium, 304.
cysticercus of, in myocardium, 466.
Testicle, syphilis of, 32.
Tetanoid chorea, 695.
Tetanus, bacillus of, 206.
conveyance of, 206.
factors influencing prognosis of, 207-208.
injection in, 206.
injections of magnesium sulphate in, 209.
symptoms of, 207-208.
Tetany, associated with acute infections, 1167.
characteristic features of, 1165.
definition of, 1165.
essential factor of, 1166.
forms of, 1166.
from poisons, 1167.
prognosis of, 1167.
gastric, 1167.
gastro-intestinal, 1167.
idiopathic, 1166.
characteristic features of, 1166.
prognosis of, 1167.
remissions of, 1166.
in gastric ulcer, 596.
occurrence of, 1166.
of maternity, 1168.
of nervous diseases, 1168.
of parathyroid disturbance, 1168.
Thermic fever, 1206.
Third nerve, paralysis of, 860.
Thirst, in diabetes mellitus, 1114.
Thomsen's disease, 1085.
Thrombo-endocarditis septica, 471.
Thrombo-endocarditis simplex, of Ziegler, 469.
Thrombomyoendocarditis, 285.
Thrombosis, and liver cirrhosis, 697.
cerebellar, 1004.
cerebral, 953.

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Thrombosis, in arteriosclerosis, 418.
in typhoid fever, 95.
of hepatic artery, 680.
of hepatic vein, 679.
of marasmus, 679.
pulmonary, with chlorosis, 518.
septic, 132.
spinal, 929.
tuberculous, 275.
Thymic asthma, 1164.
"Thymus death," 1145-1164.
Thymus gland, disease of, atrophy, 1164.
hypertrophy, 1163.
in hyperthyroidea, 1145.
with Hodgkin's disease, 1164.
status thymo-lymphaticus, 1164.
sarcoma of, 1164.
Thyroid extract, glucosuria produced by, 1107.
in Raynaud's disease, 1073.
Thyroid gland, complete loss of function of, 1157.
function of, 1154.
goiter, 1137, 1139.
insufficiency, 1153.
classification of, 1154.
dangers of, 1154.
in adults, 1155.
in children, 1154.
maximal, 1154.
total extirpation of, 1155.
tuberculosis, 249.
tumors, 1136.
and hyperthyroidea, 1150.
inflammatory conditions of, 1136.
Thyroiditis, 1136.
acute swelling with, 1137.
productive or sclerotic, 1137.
Tic convulsive, blepharospasm with, 867.
clonic and tonic spasms in, 867.
definition of, 867.
following trigeminal neuralgia, 867.
longevity in, 867.
other neuroses with, 867.
Tic douloureux, causes of, 842.
operative interference and injections for, 842.
Tic habit, due to facial spasm, 866.
Tinnitus aurium, with aural paralysis, 868.
Tobacco, arteriosclerosis due to, 407.
Tongue, tuberculosis of, 252.
Tonsillitis, acute follicular, 293.
epidemic, 294.
sporadic, 293.
albuminuria with, 747.
chronic, 299.
complications in, arthritis, 296.
heart, 294.
kidney, 296.
paralysis, 296.
pneumonia, 297.
septicemia, 296.
various, 297.
epidemic, complications in, 294-295.
Tonsillitis, epidemic, course of, 295.
due to infected milk, 294.
phlegmonous, 297.
septic, 297.
streptococcus, 293.
accompanying other diseases, 294.
endemic and epidemic, 294.
mortality from, 297.
symptoms of, in acute follicular, 293.
Vincent's angina in, 298.
Tonsils, acute infections of, 293.
as port of entry for infection, 292.
disease, and chorea, 1039.
enlarged, influence of, on growing child, 299.
enucleation of, 292-293.
in tuberculosis, 292.
mortality due to diseases of, 300.
primary focus for disease, 292.
tuberculosis of, 252.
Torticollis, causes of, 873.
congenital, 873.
tenotomy for, 873.
course of, 873.
functional or spasmodic, 872.
hysterical, 1019.
organic, 872.
psychic influence of, 873.
symptoms of, 873.
Toxinemia, 133.
Trachea, syphilis of, 33.
tuberculosis, 252.
Trapezius paralysis, 872.
spasm of, 872.
Traumatic neurosis, complex of symptoms in, 1021.
convulsive tic in, 1023.
death never due to, 1024.
diagnosis of, 1021.
due to electric shock, 1024.
due to railroad accidents, 1022.
heart affections in, 1023.
honest cases of, 1021.
leading to suicide, 1024.
litigated cases of, 1021-1022.
localized muscular spasm in, 1023.
mental attitude in, 1023.
multiple and single symptoms, 1023.
neurotic-psychic symptoms of, 1022.
persistent melancholia of, 1023.
prognosis of, principal facts in, 1022.
psychic attacks in, 1023.
psychic disturbances in, 1024.
surgical conditions in, 1023.
syphilis associated with, 1024.
with organic injury, 1023.
without litigation, 1023.
vasomotor symptoms in, 1023.
Traumatism, epilepsy due to, 1050.
glucosuria due to, 1108.
influence of, on development of general paralysis, 1024.
migraine due to, 1060.

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Trematodes, 316.
complications with, 316.
nature of, 316.
symptoms of, 316.
Tremor, in exophthalmic goiter, 1144.
in lead encephalopathy, 1190.
Treponema pallidum, 15.
carriers of, 70.
excursion of, through blood, 19.
in metasyphilitic disease, 44-45.
Trichinosis, 312.
Trichocephalus dispar, 312.
Tricuspid insufficiency, 503.
Tricuspid stenosis, 503.
Trigeminus, neuralgia of, 841.
paralysis of, 862.
symptoms of, 862.
Trophedema, hereditary, 1080.
Trophoneurosis, hysterical, 1018.
Tropical sore or ulcer, 83.
Tropical splenomegaly, 83.
Trypanosomiasis, 81.
Tube casts, 749.
Tubercula dolorosa, 884.
Tuberculin, 225.
in pulmonary tuberculosis, 238-239.
Tuberculoma, 251.
Tuberculosis, abortion in, 241.
acute miliary (general), meningeal form of, 224-225.
primary focus for, 223.
pulmonary form of, 224.
secondary character of, 222.
spread of, 223.
typhoid form of, 223.
advance in study of, 217-220.
and malaria, 78.
and marriage, 241.
and pneumonia, 163-164.
bacillus of, 216.
bovine, 219.
bronchial, 252.
bronchial asthma and, 371.
cardiovascular, 274.
catarrhal, 250.
complications in, alcoholism, 242.
diabetes, 242.
exophthalmic goiter, 242.
gangrene of lung, 242.
gouty conditions, 242.
meningitis, 242.
obesity, 242.
syphilis, 242.
diminished mortality from, 218-219.
fibroid phthisis in, 244.
galloping, 227.
genital, in female, 271.
genito-urinary, 267.
heredity as factor in, 220, 221, 241.
history of, 217-220.
immunity of normal tissue to, 218.
in early life, 240-241.
in influenza, 127.
in tabes dorsalis, 58.
infection of child with, by mother, 220, 241.
Tuberculosis, inviting conditions for, 221-222.
ischiorectal, 257.
Kossel's conclusions on, 219.
laryngeal, 250.
mesenteric, 266.
migraine and, 1060.
nasal, 250.
nursing of baby by mother with, 241.
of aorta, 274.
of appendix, 656.
of brain, 996.
of digestive tract, esophagus, 253.
intestinal, 253.
lips, 252.
stomach, 253.
tongue, 252.
tonsils, 252.
of gall-bladder, 256.
of liver, amyloid degeneration, 255.
cirrhosis of liver and, 255.
fatty degeneration, 255.
primary tubercle nodule, 256.
of lymphatic glands, 265.
of myocardium, 275.
of nervous system, 277.
of pancreas, 262.
of parotid, 249.
of spinal cord, 924.
of thyroid, 249.
predispositions to, 220-221.
pregnancy in, 241.
pulmonary. See Pulmonary Tuberculosis.
in typhoid fever, 99.
in whooping-cough, 188.
renal, 268.
resemblance to, of lymphoblastoma, 537.
röntgenoscopy for, 239-240.
spinal leptomeningitis due to, 934.
splenic, 262.
suggested by orthostatic albuminuria, 745.
suprarenal, 263.
symptoms of, blood pressure, 276.
constriction of veins, 276.
dyspepsia, 253.
heart, 276.
pulse, 276.
tests for, lumbar puncture, 225-226.
tuberculin, 225.
tonsils in, 292.
tracheal, 252.
transmission of, 219-220.
tuberculin tests for, 238-239.
with cirrhosis, 693.
with diabetes mellitus, 1118.
Tuberculous abscess of brain, 981.
Tuberculous endocarditis, 275.
Tuberculous enteritis, chronic, 254.
intestinal stricture with, 255.
primary, 253.
secondary, 254.
Tuberculous laryngitis, 234, 241, 251.
Tuberculous meningitis, 277.
in measles, 345.

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Tuberculous meningitis, invasion of cranial nerves in, 278.
Tuberculous myelitis, 277.
Tuberculous nephritis, hematuria due to, 759.
Tuberculous neuritis, 278.
Tuberculous pachymeningitis, 277.
Tuberculous pericarditis, 274.
Tuberculous peritonitis, chronic, 259.
chronic fibroid, 260.
focus of, 257.
miliary, 258.
surgical treatment of, 260-261.
Tuberculous pleurisy, 389.
adhesions in, 248.
complications in, 248-249.
development of, 247.
dry, 248.
frequency of effusion in, 248.
history of, 247.
Tuberculous pneumonia, 244.
Tuberculous pyloric stenosis, 584.
Tuberculous spleen, 1170.
Tuberculous thrombosis, 275.
Tumors, of brain. See Brain Tumor.
of cauda equina, 926.
of conus, 926.
of peripheral nerves, 883.
of spinal cord, classification of, 918.
differentiation between extra- and intra-medullary, 923.
due to carcinoma elsewhere in body, 919-920.
early diagnosis of, 924.
extramedullary, benign and slow growth of, 920-921.
cervical invasion by, 922.
focal symptoms of, 921.
in dorsal region, 922.
intervertebral, extradural, 919.
intradural, 919.
laminectomy for, 922.
neuralgia with, 921.
paralyses with, 921-922.
reflexes in, 921.
sciatic pain with, 921.
sensory symptoms of, 921.
vertebral, 919.
without cachexia, 921.
intramedullary, 919.
carcinoma, 924.
compression myelitis in, 925.
direction of growth of, 922.
early diagnosis of, 922.
echinococcus and cysticercus cysts, 924.
glioma, 924-925.
infiltrating and limited, 923.
metastasis to spine and cord, 925.
multiple neuromata, 924.
primary or secondary, 924.
sarcoma, 923.
secondary chronic, 925.
spinal gliomatosis in, 925.
surgical removal of, 922-923, 925.
transverse myelitis in, 925.
Tumors, intramedullary, tubercle, 924.
lumbar puncture in, 926.
necessity of surgery for, 918.
relation of trauma to, 925.
x-ray in, 925.
Tympany, in typhoid fever, 102.
Typhlatonia, 632.
Typhlectasia, 632.
Typhlitis, 644.
Typhlitis stercoralis, 635.
Typhoid appendix ulcers, 650.
Typhoid fever, abortive, 90.
afebrile, 92.
age in, 87.
albuminuria of nephritis in, 108.
alcoholics with, 111.
alimentary disturbances in, diarrhea, 102.
gastric, 102.
intestinal hemorrhage, 102, 103, 103.
of mouth, 101.
parotitis, 101.
peritonitis, 104.
tympany, 102.
ambulatory, 91.
appendicitis with, 657.
blood in, 99-100.
blood count in, 88.
"carriers" of, 85.
cause of infection by, 84.
causes of death in, 114-115.
cerebral invasion by, 111.
circulatory disturbances in, accented aortic II sound, 95.
blood pressure, 94.
bradycardia, 95.
cyanosis, 93.
endocarditis, 96.
heart, 94.
pericarditis, 96.
post-typhoid myocarditis, 95.
pulse, 93.
sudden death from, 94.
thrombosis, of arteries, 96.
gangrene from, 96.
phlebitis cruralis, 95-96.
deaths from sequelae of, 115-116.
ear complications in, 113.
encephalitis in, 974.
epidemics of, 88.
eye complications in, 113.
factors influencing prognosis of, 86.
genito-urinary disturbances in, albuminuria, 108, 109, 110.
cystitis, 109.
gangrene of vulva, 110.
menstruation, 110.
nephritis, 108-109.
orchitis, 110.
pregnancy, 110.
pyelitis, 110.
urine, 107.
immunity to, through vaccination, 85.
influence of complications of, 88.

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Typhoid fever, intestinal hemorrhage in, 102.
death due to, 104.
prognostic significance of, 103.
relapses of, 103.
liver and bile passages in, cholecystitis, 105.
jaundice, 105.
malignant infection of, 88.
manifestations of, circulatory, 93.
general, 87-88.
temperature and pulse, 89.
mild irregular, 90.
mortality from, 86.
muscular system in, 113.
nervous system in, central, 111.
convulsions, 112.
delirium, 111.
peripheral, 112.
reflexes, 112.
treatment of, 112.
osseous system in, 113.
peritonitis in, 104.
perforative, 104-105.
post-typhoid pyrexia from, 93.
protracted fever in, 89-90.
pulse in, 89-97, 93.
reactions in, 110.
relapses of, 114.
resistance of patient to, 87.
respiratory disturbances in, bronchitis, 98.
catarrhal pharyngitis and laryngitis, 97.
epistaxis, 97.
hypostatic congestion, 98.
lung abscess, 98.
pneumonia, 98.
pneumothorax, 99.
pulmonary edema, 99.
pulmonary infarct, 98.
pulmonary tuberculosis, 99.
purulent pleurisy, 99.
respiration, 96.
severity of infection in, 87-88.
skin disturbances in, abscesses, 106.
alopecia and atrophic changes, 106.
bedsores, 106.
erysipelas, 107.
miliary eruption, 106.
phlegmons, 107.
purpura hemorrhagica, 106.
roseola, 106.
spleen in, 107.
sudden death in, 94.
symptoms of perforation in, 93.
temperature in, 89-97.
sudden fall of, 92-93.
Typhoid spine, 112.
Typhoid symptoms, in gonococcus endocarditis, 190.
in influenzal fever, 130.
in malarial fever, 74.
in tuberculosis, 223.
Typhus abortions, 91.
Typhus exanthematicus. See Typhus fever.
blood in, 119.
general symptoms of, 119-120.
history of, 117, 118, 119.
prevention of, 118-119.
pulse in, 119.
urine in, 120.
without intestinal lesions, 114.
Typhus levissimus, 90.

U

Ulcers, catarrhal follicular, 621.
decubitus, of esophagus, 564.
peptic, of esophagus, 564.
gastric, 585.
Ulnar paralysis, causes of, 879.
Uremia, acute, abnormally high temperature with, 764.
active mania with, 764.
cerebral paralysis with, 764.
chronic nephritis with severe headaches and, 765.
diarrhea with, 765.
hemiplegia with, 764.
dyspnea with, 765.
prognosis of, 763.
pulmonary edema with, 764.
pulse condition in, 765.
renal sufficiency tests in, 763.
retinal hemorrhages with, 765.
sudden blindness before attack of, 764.
symptoms of, 763.
test for impairment of function in, 771.
typhoid state associated with, 765.
vomiting with, 764.
with chronic nephropathies, 763.
with respiratory paralysis, 764.
chronic, diagnosis of, 767.
symptoms of, 766-767.
due to hydronephrosis, 818.
in cirrhosis, 694.
in chronic nephritis, 799.
in nephritis, 792.
in scarlet fever, 331.
latent, anuria with, 765.
leading features of symptom-complex of, 762.
nature of, 762.
Uremic breath, 767.
Ureter, stones in, 822.
Uric acid diathesis, 785.
Urinary fistulae, with gall-stones, 730.
multiple, due to trematodes, 317.
Urinary secretions, anomalies of, albuminuria, 741.
alkaptonuria, 786.
bacilluria (bacteriuria), 774.
casts, 749.
chyluria, 776.
cystinuria, 785.
hematoporphyrinuria, 787.
hematuria, 753.

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Urinary secretions, anomalies of, hemoglobinuria, 761.
indicanuria, 780.
lipaciduria, 787.
lipuria, 777-787.
lithuria, 785.
melanuria, 786.
oxaluria, 779.
phosphaturia, 777.
pneumaturia, 787.
uremia, 762.
urobilinuria, 782.
Urine, albumin in, 741.
alkaptonic, 786.
ammoniacal fermentation of, 778.
black, 786.
blood in, 753.
casts in, 749.
complete suppression of, 766.
cryoscopy, 774.
cystin in, 785.
disease-producing germs in, 774.
fat in, 776, 777, 787.
gas in, 787.
hematin in, 787.
hemoglobin in, 761.
indican in, 780.
in amyloid kidney, 815.
in chronic interstitial nephritis, 808.
in chronic nephritis, 800.
in diabetes mellitus, 1116.
indol in, 780.
indoxylsulphate of potassium in, 780.
in leukocytic leukemia, 531.
in measles, 343.
in neurasthenia, 1029.
in paratyphoid, 123.
in pernicious anemia, 527.
in pyelitis, 833.
in tuberculosis, 234.
in typhoid fever, 107.
methemoglobin in, 761.
oxalic acid in, 779.
phosphates in, 777.
serum albumin in, 741.
serum globulin in, 741.
triple phosphates in, 778.
uric acid in, 785.
urobilin in, 782.
volatile fatty acids in, 787.
Urobilinuria, clinical significance of, 782.
conditions associated with, 783-784.
prognostic significance of, 782-783.
Urogenital disease, renal sufficiency tests for, 768.
Urticaria, bronchial asthma with, 369.
giant. See Angioneurotic edema.
Uterine tuberculosis, 273.

V

Vaccination, against hay fever, 359.
against smallpox, 333.
influence of, on prognosis, 340.
rules for, 339-340.
Vaccination, in typhoid fever, 85.
Vaccine treatment, for gonococcus arthritis, 192.
Vaccinia, for smallpox, 339.
Vaginal tuberculosis, 273.
Vagotonia, due to atropin, 1082.
due to pilocarpin, 1082.
prognosis of, 1083.
symptoms of, 1082.
Vagotonic asthma, 371.
Vagus paralysis, 871.
Valvular disease, aortic insufficiency, 500.
aortic stenosis, 499.
blood pressure in, 496.
chronic, prognosis of, 495.
combined, 504.
defects of pulmonary valve, 503.
due to mitral insufficiency, 495.
due to mitral stenosis, 497.
general considerations, in prognosis of, 478.
influence on, of marriage and pregnancy, 486, 487, 488.
localization of, 495.
lung complications in, 497.
pulmonary insufficiency in, 504.
rupture in, 500.
tricuspid insufficiency, 503.
tricuspid stenosis, 503.
Vaquez disease. See Erythremia.
Varicella, complications in, 342.
death due to, 341.
nature of, 341.
nephritis in, 342.
prognosis of, 341.
Varicocele, operation for, in neurasthenia, 1029.
Variola hemorrhagica, purpura variolosa, 337.
pustulosa, 337.
Variola vera, 336.
Varioloid, 337.
Vascular spasm, anemia of brain due to, 947.
in arteriosclerosis, 414.
in lead poisoning, 1190.
Vasomotor and trophic disturbances, acroparesthesia, 1074.
adiposis dolorosa, 1078.
angioneurotic edema, 1075.
ataxia, 1079.
dropsy (intermittent) of joints, 1079.
edema of legs, persistent hereditary, 1080.
erythromelalgia, 1066.
hysterical, 1018.
in traumatic neuroses, 1023.
Raynaud's disease, 1069.
scleroderma, 1077.
Venous obstruction, in brain tumor, 996.
Venous stasis, congested kidney due to, 813.
Vertigo, acute, of gastrohepatic and intestinal origin, 870.
aural, 869.

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Vertigo, due to constitutional disease, 870.
due to organic brain disease, 870.
epilepsy and, 870.
essential, 870.
general considerations of, 870.
in brain tumor, 992.
in multiple sclerosis of brain and cord, 910.
in tabes dorsalis, 59.
ocular associated with diplopia, 870.
petit mal with, 870.
stomachal, in chronic gastritis, 578.
in dilatation of stomach, 578.
of Trousseau, 870.
Vestibular nerve, involvement of, in auditory paralysis, 869.
Vicarious menstruation, pulmonary hemoptysis of, 376.
Vincent's angina, 298.
Visceroptosis, 579.
Visual field, hysterical contraction of, 1011.
Vocal cords, hysterical paralysis of, 1014.
Volvulus, 637.
Vomiting, in acute biliary colic, 722.
cerebral, 993.
fecal hysterical, 1018.
hysterical, 1017.
in brain tumor, 992.
in amyloid kidney, 815.
in nephritis, 792, 798.
in pneumonia, 161.
nervous in hypermotility, 617.
of cancer, 604.
Vulva, diphtheria of, 138.
gangrene of, in typhoid, 110.

W

Walking typhoid, 91, 92.
Wassermann reaction, in paresis, 63.
in syphilis, negative, 19, 21.
positive, 15, 18, 21, 22, 28.
in tabes dorsalis, 57.
Weil's disease, 350.
Werlhof's disease, 544.
Westphal symptom, of tabes dorsalis, 55.
"Wet brain," in delirium tremens, 1184.
Whip worm, 312.
Whooping-cough, blood condition in, 189
character of, 186.
complications in, 186, 189.
conclusions on, 189.
stages of, 186.
uncomplicated, 186.
with measles, 344.
Woolsorters' disease. See Anthrax.
Writers' cramp, 1064.
Wryneck. See Torticollis.

X

X-ray for adherent pericardium, 431.
in aneurism, 422.
in arteriosclerosis, 419.
in biliary colic, 723.
in brain tumors, 999.
in dilatation of colon, 640.
in early diagnosis of cancer, 602.
in endocarditis, 492.
in gastric ulcer, 589.
in leukemia, 535.
in nephrolithiasis. 821.
in pericarditis, 428.
in pyelitis, 832.
in pyloric obstruction, 584.
in tumors of spinal cord, 925.

Y

Yellow fever, conveyance of, 347.
epidemics of, 347.
factors in prognosis of, 347-348.
nature of, 347.
prophylaxis against, 347.
racial insusceptibility to, 348-349.
symptoms of, 347-348.

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